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In

Clinical Haematology

For the examinations to be conducted in August 2014

Department of Clinical Haematology

Christian Medical College, Vellore.

Tamil Nadu, India.

Evaluation of Berlin-Frankfurt-Munster (BFM) protocols in acute lymphoblastic leukemia and the role of flow cytometry in minimal residual disease monitoring: A single tertiary centre analysis from India.

CERTIFICATE

This is to certify that the dissertation entitled 'Evaluation of Berlin-Frankfurt-Munster (BFM) protocols in acute lymphoblastic leukemia and the role of flow cytometry in minimal residual disease monitoring: A single tertiary centre analysis from India' is a bonafide work of the candidate, Punit Lalchand Jain, of Christian Medical College in partial fulfillment of the University rules and regulations for award of Doctorate of medicine (higher specialty) in Clinical Haematology under my guidance and supervision during the academic year 2011-2014.

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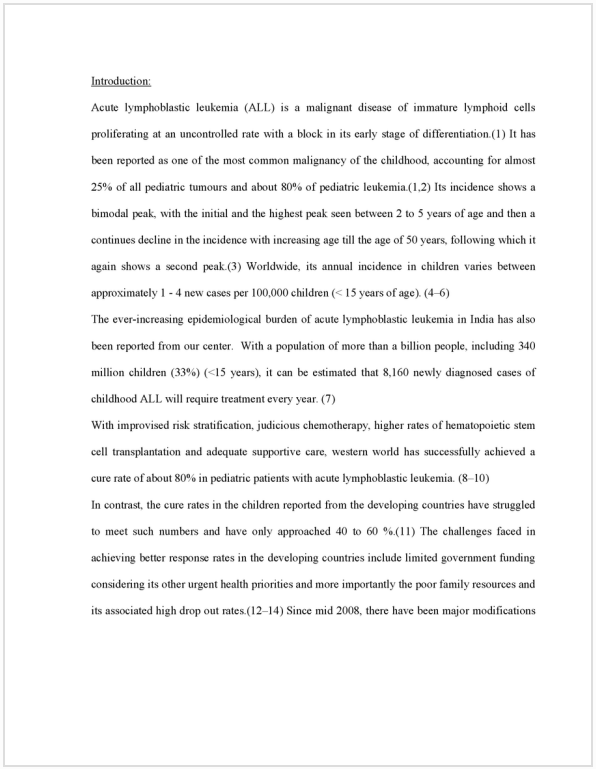

Introduction:

Acute lymphoblastic leukemia (ALL) is a malignant disease of immature lymphoid cells proliferating at an uncontrolled rate with a block in its early stage of differentiation.(1) It has been reported as one of the most common malignancy of the childhood, accounting for almost 25% of all pediatric tumours and about 80% of pediatric leukemia.(1,2) Its incidence shows a bimodal peak, with the initial and the highest peak seen between 2 to 5 years of age and then a continues decline in the incidence with increasing age till the age of 50 years, following which it again shows a second peak.(3) Worldwide, its annual incidence in children varies between approximately 1 - 4 new cases per 100,000 children (< 15 years of age). (4–6)

The ever-increasing epidemiological burden of acute lymphoblastic leukemia in India has also been reported from our center. With a population of more than a billion people, including 340 million children (33%) (<15 years), it can be estimated that 8,160 newly diagnosed cases of childhood ALL will require treatment every year. (7)

With improvised risk stratification, judicious chemotherapy, higher rates of hematopoietic stem cell transplantation and adequate supportive care, western world has successfully achieved a cure rate of about 80% in pediatric patients with acute lymphoblastic leukemia. (8–10)

In contrast, the cure rates in the children reported from the developing countries have struggled to meet such numbers and have only approached 40 to 60 %.(11) The challenges faced in achieving better response rates in the developing countries include limited government funding considering its other urgent health priorities and more importantly the poor family resources and its associated high drop out rates.(12–14) Since mid 2008, there have been major modifications

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October 9, 2012

Dr. Punit Jain
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Department of Clinical haematology
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Dear Dr. Punit Jain,

Sub: **Fluid Research grant project NEW PROPOSAL:**
Evaluation of BFM protocols in acute lymphoblastic leukemia and role of minimal residual disease monitoring: A Single tertiary centre analysis from India.
Dr. Punit Jain, PG Registrar, Clinical Haematology, Dr. Vikram Mathews, Dr.Alok Srivastava, Dr. Biju George, Dr. Auro Viswabandya, Dr. Aby Abraham, Dr. Rayaz Ahmed, Clinical Haematology.

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I enclose the following documents:-

1. Institutional Review Board approval
2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Vikram Mathews, Professor, Department of Haematology, CMC

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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

A sum of Rs 40,000/- (Rupees Forty thousand only) will be sanctioned for 12 months. A subsequent installments of 40,000/- each will be released at the end of the first year following the receipt of the progress report (Total amount 80,000/-).

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Vikram Mathews, Professor, Department of Haematology, CMC

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Last but not the least, my gratitude to the patients and families whose data has been analyzed in this study.

CONTENTS

ABSTRACT:

Title: Evaluation of Berlin-Frankfurt-Munster (BFM) protocols in acute lymphoblastic leukemia and the role of flow cytometry in minimal residual disease monitoring: A single tertiary centre analysis from India.

Department: Clinical Hematology, Christian Medical College, Vellore.

Name of candidate: Dr. Jain Punit Lalchand.

Degree and subject: D.M. Clinical Hematology

Name of the guide: Dr. Vikram Mathews, Professor, Department. of Clinical Hematology.

Aims and Objectives of the study: (1) To study the clinical profile of children and adults diagnosed with acute lymphoblastic leukemia in our institute and their treatment outcome, when treated with different BFM protocols (2) To evaluate the clinical outcome in adolescent patients with acute lymphoblastic leukemia between 15 - 20 years of age, by using pediatric treatment regimens instead of adult regimens as currently used. (3) To assess the role of minimal residual disease status monitoring by flow cytometry at time of documenting remission, post induction phase of chemotherapy.

Methodology: For retrospective analysis of adult patients, we included all newly diagnosed patients with acute lymphoblastic leukemia from January 2004 to February 2014. For adolescent patients, we compared adolescents treated by adult regimens from January 2004 to June 2012 with those adolescents treated with pediatric regimens from July 2012 to February 2014. We also compared standard and intermediate risk pediatric patients treated with the non BFM 95 regimens from January 2004 to those receiving BFM 95 based regimens from 2008. Lastly, since July 2012 we prospectively analyzed the role of flow cytometry in assessing the minimal residual status at the end of induction chemotherapy and compared the outcomes of those who tested positive with those tested

negative.

Results: Among 455 adults analyzed, there were 331(72.7 %) standard risk and 124 (27.2 %) high risk adults. Median follow up duration was 65 months. There were 132 (29 %) relapses and 179 (39.3 %) deaths. The 5 year EFS was 50.1 ± 2.9 % and the 5-year OS was 51.6 ± 2.9 %.
Among children with standard risk ALL, with an actuarial median follow up period of 25(1.5 - 65) months and 17(1- 64) months for those treated with the BFM 95 protocol and those with the Non MTx/Non RT based study protocol; the three year event free survival was 95 ± 4.9 % and 86.5 ± 6.5 % respectively. (*P* value= 0.391). Among children with intermediate risk ALL, with an actuarial median follow up period of 27 (1 - 47) months and 18 (1-116) months for those treated with the BFM 95 protocol and those with the radiation (RT) based protocol; the two year overall survival was 96.9 ± 3.1 % and 85.6 ± 2.4 % respectively. (*P* value = 0.103)_With an actuarial median follow up period of 7.7 (1 - 19) months and 18(1-118) months those treated with intermediate risk pediatric protocol and the modified adult GMALL protocol; the one year event free survival was 82.3 ± 7.3 % and 75.9 ± 3.6 % respectively.(*P* value = 0.752) Among patients tested for the minimal residual disease, with an actuarial median follow up of 7.7 (1-19) months, the 6 months and 1 year EFS in MRD (-) cohort (n = 53) is 97.4 ± 2.6 %. With an actuarial median follow up of 7.7 (1-13) months, the 6 months and 1 year EFS in MRD (+) cohort (n = 16) is 75 ± 21.7 %. With a median follow up of 6 months, the 6 months OS in MRD strongly (+) cohort (n = 6) is 20 ± 17.9 %. (P = 0.000)

Conclusions: I] Using the current modified GMALL and BFM 95 regimens in adults (≥ 15 years) and children (>1<15 years), treatment outcomes were comparable to those reported in the international literature. There was no significant difference as yet in the BFM 95 and the non BFM 95 regimens. II] Using pediatric regimens in adolescent age group (≥15 ≤ 20 years) did not reveal any significant difference in overall outcome as compared to adult regimens. Though the follow up is short, pediatric regimens are feasible in adolescents with minimal toxicity and there appears to be a trend towards improvement in their outcomes with pediatric regimens. III] Using flow cytometry in detecting minimal residual disease can significantly identify high risk patients and improve their outcome by timely intensification.

Keywords: GMALL, BFM 95, MRD.

Introduction:

Acute lymphoblastic leukemia (ALL) is a malignant disease of immature lymphoid cells proliferating at an uncontrolled rate with a block in its early stage of differentiation.(1) It has been reported as one of the most common malignancy of the childhood, accounting for almost 25% of all pediatric tumours and about 80% of pediatric leukemia.(1,2) Its incidence shows a bimodal peak, with the initial and the highest peak seen between 2 to 5 years of age and then a continues decline in the incidence with increasing age till the age of 50 years, following which it again shows a second peak.(3)

Among adults with ALL, although the complete remission rates (CR) have approached 74% to 93 %, the overall survival rates has only approached 27% to 54%.(4) These response rates are much lower than the response rates achieved in children, which is close to 80 %. (5,6) There are multiple reasons for these differences, though they have been mainly attributed to the higher occurrence of poor risk cytogenetics, along with a reduction in incidence of the favourable cytogenetics and a poor tolerability to chemotherapy with increasing age. Also, the adult leukemic blasts have been shown to be more resistant to chemotherapy. (7)

Among younger adults with ALL, there have been significant changes in the overall survival in comparison to the older adults. An improvement in the relative survival rates in the age group of 15-19 years from 41.0% to 61.1% at 5 years, and from 33.0% to 60.4% at 10 years has been reported.(8)

The response rates in adults ≥ 15 years from our institute, treated using a modified GMALL protocol between 1994 to 2003 have also been published, showing a CR rate, a 5 year Kaplan Meier estimate of OS, EFS and a DFS of 38%, 36% and 44% respectively.(9)

Among children (<15 years), the annual incidence of ALL varies between approximately 1 - 4 new cases per 100,000 children (< 15 years of age). (10–12) India has a population of more than a billion people, including 340 million children (33%) (<15 years) and it can be estimated that 8,160 newly diagnosed cases of childhood ALL will require treatment every year. (13)

With improvised risk stratification, judicious chemotherapy and adequate supportive care, western world has successfully achieved a cure rate of about 80% in pediatric patients with acute lymphoblastic leukemia. (5, 6, 14)

In contrast, the cure rates in the children reported from the developing countries have struggled to meet such numbers and have only approached 60 %.(15, 16) In our institute, treatment of children < 15 years of age has traditionally been on the lines of pediatric BFM regimens. The success of the treatment of pediatric patients with acute lymphoblastic leukemia from our institute using BFM based protocols is reflected in the achievement of a 5 year Kaplan Meier estimate of overall survival (OS) of 59.8%, event free survival (EFS) of 56%, and disease free survival (DFS) of 53.9%.(16)

The challenges faced in achieving better response rates in the developing countries include limited government funding considering its other urgent health priorities and more importantly the poor family resources and its associated high dropout rates.(17–19)

Since mid 2008, there have been major modifications in the treatment protocols of the pediatric population in our institute. From mid 2008, the BFM protocols for the pediatric population < 15 years of age have been changed from the 76/79-based regimens to the BFM 95 based regimens for children of the same age group.

These changes were implemented in an effort to improve the clinical outcomes and achieve results on par with those achieved in developed countries. Since the introduction of these changes, no systematic analysis has not been done to assess if the anticipated improved clinical outcomes were achieved. The present study will analyze the response rates of the children treated between 2008 to February 2014 by the BFM 95 protocol and compare its response rates with the previously used non BFM 95 regimens.

Review of literature:

The earliest classification of ALL was the French American British (FAB) classification, which traditionally described three classes of ALL (L1, L2, and L3) (20–22). This classification did not describe the genetic behavior, the Immunophenotype or the clinical behavior of the disease, thus was deficient in adequately prognosticating the disease.

Subsequently, a classification of ALL based on type of cell lineage (B or T), using monoclonal antibodies in the form of immunophenotyping was proposed. ALL blasts were traditionally classified into precursor–B-cell types, mature–B-cell ALL, and T-lineage ALL on the basis of immunophenotyping, each having its individual prognostic significance. (23) About 85% of pediatric ALL are reported to be of B-lineage phenotype, while the rest are of the T-lineage.(24)

At present, ALL classification has evolved from the traditional FAB to the present WHO 2008, which has incorporated morphology, immunophenotyping as well as cytogenetics, to determine the lineage and stratify the disease. (25) According to the WHO 2008, ≥ 20% blasts in the bone marrow are sufficient for the diagnosis of ALL.

[I] Adult ALL:

Based on published literature worldwide, although the complete remission rates in the adults diagnosed with acute lymphoblastic leukemia have approached 74% to 93 %, the overall survival rates has only approached 27 % to 54 %.(26) The results of adult ALL (15 years and above) treated with a modified GMALL protocol earlier from our institute from a period between 1994 to 2003 has been published, with the estimated 5 year overall survival, event free survival and disease free survival being 38%, 36% and 44% respectively.(9) There are significant changes in the biology of the disease with an increasing age. Listed below in table 1 are the relevant prognostic factors in adult acute lymphoblastic leukemia.(26)

Prognostic factors:

(i) Age – It shows a perpetual decline in survival with an advancing age. The OS for adults < 30 years has been shown to be between 34% to 57% v 15% to 17% for > 50 to 60 years of age. (27–31)

(ii) Elevated WBC at presentation has been considered as a poor prognostic factor.(32) A WBC > 30,000 in B cell ALL has been shown to have an OS between 19 to 29 %. (28, 33)

(iii) Comparatively, T-lineage ALL shows a better outcome when compared to B-lineage ALL. The leukemia free survivals also differs according to the subtypes in T cell ALL Early T-ALL - 25%, Thymic (cortical T-ALL) - 63% and mature T-ALL— 28%.(28, 34)

(iv) Other significant factors include:

(a) Sensitivity of ALL cells to corticosteroids and the chemotherapy in vitro. (35, 36). ALL cells in adults are less sensitive to prednisone, vincristine, and L-asparaginase

unlike in children. (7)

(b) Deteriorating organ function with age, thereby affecting the metabolism of the drugs.

(c) Higher incidence of infections, organ dysfunctions, treatment delays and omissions in chemotherapy medications. (37)

Table 1: Relevant prognostic factors in adult ALL (26)

	FAVOURABLE	**ADVERSE FACTORS**	
Age	<25 yr., <35 yr.	>35 yr., >55 yr., >70 yr.	
At Diagnosis		B Lineage	T Lineage
WBC Count at diagnosis	< 30,000/μL	> 30,000/μL	> 100,000/μL
Immuno-Phenotype	Thymic T	Pro-B ($CD10^{--}$) Pre-B ($CD10^{--}$)	Early T ($CD1a^{--}$, $sCD3^{--}$) Mature T($CD1a^{-}$,SCD3 +)
Cytogenetics	TEL-AML1 (?) Hyperdiploidy (?)	t (9;22)/BCR-ABL t (4;11)/ALL1-AF4 Complex karyotype Low Hypodiploidy/ Near tetraploid (?)	 Complex Karyotype Low Hypo diploid/ Near tetraploid (?)
Others **1. Prednisone response** **2. MRD after Induction chemotherapy**	 Good (?) Negative/ $<10^{-4}$	 Poor (?) Positive $>10^{-4}$	

The overall outcomes reported in various trials are shown in table 2 below:

Table 2: Major adult ALL trials: (26)

Study	Year	N	Median age, Year (range)	CR Rates	Survival (year)
CALGB9 111, USA	1998	198	35 (16-83)	85%	40% (3 yr)
LALA 87, France	2000	572	33 (15-60)	76%	27% (10 yr)
GMALL 05/93, Germany	2001	1,163	35 (15-65)	83%	35% (5 yr)
MD Anderson, USA	2004	288	40 (15-92)	92%	38% (5 yr)
MRC XII/ ECOG E 2993, UK-USA	2005	1,521	15-59	91%	38% (5 yr)
GIMEMA 0496, Italy,	2005	450	16-60	80%	33% (5 yr)
Pethema ALL-93, Spain	2005	222	27 (15-50)	82%	34% (5 yr)
GMALL 07/03	2007	713	34 (15-55)	89%	54% (5yr)

Abbreviations: **CALGB**, Cancer and Leukemia Group B; **LALA**, leucémie Aiguë Lymphoblastique de l'Adulte; **MRC**, Medical Research Council; **NOPHO**, Nordic Society of Pediatric Hematology and Oncology; **GIMEMA,** Gruppo Italiano Malattie EMatologiche dell'Adulto; **GMALL,** German Multicentre study group for Adult ALL; **PETHEMA,** Programme for the Study and Treatment of Hematological Malignancies.

[II] Adolescent ALL:

About 5,000 to 6,000 cases of ALL occur in the United States every year, with about 50% of them being < 20 years old. Lately, there is improvement in the overall survival rates for ALL in all ages except for those > 60 years. The outcome in the adolescent and young adults has improved, but still lags behind the survival and outcome rates in the children. (8, 38)

The treatment response rates in adolescent ALL using a modified GMALL protocol from our institute have already been published.(9) Age has had a significant impact on survival with 5 year EFS of 46.7% for patients between 15 to 20 years, 33.38% for patients between 20 - 30 years and 14% for patients > 40 years of age (P =. 005).

Adolescents with ALL show features similar to both pediatric and adults (Table 3). (39)

Table 3: **Correlation of age with immunophenotype and cytogenetics in ALL.** (40–42)

Subgroup	**1-9**	**10-14**	**15-19**	**20-39**	**40+**
B Cell	86	68	70	60	75
T Cell	6	22	19	20	8
Ploidy:					
Normal	39	44	30	37	34
Hypo Diploid	5	8	7	6	7
Hyper Diploid	37	20	29	16	15
Cytogenetics:					
t (12; 21)	24	18	5	0	-
t (1; 19)	2	3	2	3	4
t (4; 11)	1	2	2	0	9
t (9; 22)	1	3	4	12	19

Treatment:

Several comparative studies have shown better outcomes for adolescents (15–21 years) with ALL who were treated with pediatric regimens rather than adult regimens.(43)

A) Retrospective study results: As shown in table 4.

B) Prospective Study results:

As shown in the table 5 below, several prospective studies had also evaluated the outcome of pediatric protocols in adolescent age group.(51)

[III] Pediatric ALL: (2)

The first serious attempt for categorizing ALL was proposed from the Rome Workshop in 1985. (52) Later, US National Cancer Institute (NCI) in 1993 classified ALL based on age and total count at presentation, as newer prognostic variables like cytogenetics and immunoglobulin gene rearrangement were not universally available at that time.(53)

Similarly, several other factors have been found to have important prognostic implications in the pediatric ALL.(54, 55) The commonly used risk factors for prognosticating the disease are listed in Table 6.

Table 4: Comparison of retrospective studies in adolescents and young adults with acute lymphoblastic leukemia:(44–51)						
Country	**Protocol**	**Age**	**N**	**CR (%)**	**EFS (%)**	**5 yr OS (%)**
USA (1988–2001)	CCG (P) CALGB (A)	16–20	197 124	90 90	63 34	67 (7 yr OS) 46
France (1993–2000)	FRALLE 93(P) LALA 94 (A)	15–20	77 100	94 83	67 41	78 45
Netherlands (1984–2004)	DCOG (P) HOVON (A)	15–18	47 44	98 91	69 34	79 38
Italy (1996-2003)	AIEOP(P) GIMEMA (A)	14–17	150 92	97 89	78 47	81 71
UK (1997–2002)	ALL97(P) UKALLXII (A)	15–17	61 67	98 94	65 49	71 56
Finland (1990–2004)	NOPHO (P) ALL (A)	10–25	128 97	96 97	67 60	77 70

Abbreviations: A, adult based; P, pediatric-based. **CALGB**, Cancer and Leukemia Group B; **CCG**, Children's Cancer Group; **DCOG**, Dutch Children's Oncology Group; **FRALLE**, French Acute Lymphoblastic Leukemia Group; **HOVON**, Hemato-Oncologie Voor Volwassenen Nederland; **LALA**, leucémie Aiguë Lymphoblastique de l'Adulte; **MRC**, Medical Research Council; **NOPHO**, Nordic Society of Pediatric Hematology and Oncology; **AIEOP,** Associazione Italiana Ematologia Oncologia Pediatrica; **GIMEMA** Gruppo Italiano Malattie EMatologiche dell'Adulto.

Note: p value was significant for the EFS and the OS showing a significant difference between the two study groups, except the study from Finland.

Table 5: **Comparative pediatric-based prospective studies in the adolescent and young adults**					
Country	**Protocol**	**Age**	**Number**	**CR (%)**	**EFS (%)**
USA	DFCI 91-01, 95-01	15–18a	51a	94	78
Spain	PETHEMA ALL-96	15-18 19-30	35 46	94 100	60 63
France	GRAALL-2003	15-45	172	95	58
USA	DFCI	18-50	74	82	72b
Canada	Modified DFCI	17-71	68	85	65c

a. Results restricted to adolescents. b. Estimated at 2 years. c. Overall survival.
Abbreviations:
DFCI: Dana Farber Cancer Institute; **PETHEMA**: Programa Para el Tratamiento de Hemopatías Malignas; **GRAALL**: Group for Research on Adult lymphoblastic leukemia

Table 6: (2) **Risk factors in pediatric ALL**		
Variables	**Favorable (Incidence in %)**	**Unfavorable (Incidence in %)**
Age at diagnosis	≥1 - <10 years (77%)	<1 year (3%) or ≥ 10 years (20%)
WBC at Diagnosis	≤ 50, 000/UL (80%)	≥ 50,000/UL (20%)
Immunophenotype	$CD10^{+}$ precursor B-cell ALL (83%)	$CD10^{-}$ precursor B-cell ALL (4%), T-ALL (13%)
CNS disease¶	CNS 1 (80%)	CNS 3 (3%), TLP** + (7%)
Cytogenetics	Hyperdiploidy (20%), TEL/AML1 positivity (20%)	Hypodiploidy (1%), t(9;22) or BCR/ABL positivity and t (4;11) MLL/AF4positivity (2%)
Day 8 Prednisone response (PR)	<1000/UL blood blasts (90%) in peripheral blood	≥ 1000/UL blood blasts (10%) in peripheral blood
Early bone marrow response during induction phase	< 5% blasts (M1) on Day 15 (60%)	≥ 25% blasts (M3) on day 15 (15%)
Remission status after Induction therapy (Morphologically)	< 5% blasts (M1) in bone marrow after 4 to 5 Weeks of Induction treatment (98%)	≥ 5% blasts (M2 or M3) after 4 to 5 weeks of induction therapy (2%)
Minimal residual Disease (MRD) In bone-marrow (Molecular assessment)	$<10^{-4}$ blasts after 5 Weeks of Induction Treatment – (40%)	$\geq 10^{-3}$ blasts after 12 weeks Of Treatment (Induction and Consolidation) (10%)

¶ Central Nervous System (CNS) disease criteria:(56,57)

CNS 1: Puncture nontraumatic, no leukemic blasts in cerebrospinal fluid (CSF) after cytocentrifugation.

CNS 2: Puncture nontraumatic, ≤ 5 leukocytes/L CSF with Identifiable blasts.

CNS 3: Puncture nontraumatic > 5 leukocytes/μL CSF with identifiable blasts.

** **Traumatic LP (TLP)**:

(i) TLP traumatic lumbar puncture with identifiable leukemic blasts.

(ii) A TLP with no identifiable blasts is not an adverse factor.

Differences in outcome in favourable and the unfavorable group are as listed below in Table 7.

Table 7: **Event free survival among the favourable and unfavorable factors** (58–66)		
Risk Factors	**Favourable**	**Unfavorable**
Poor Prednisolone Response (PPR)	74 – 80 %	26 - 42 %
Cytogenetics	86 - 89 %	28 – 50 %
Minimal Residual Disease (MRD)	88 - 95 %	33 - 59 %

Based on risk stratification criteria of BFM 95 group, ALL is stratified into 3 groups (table 8)

Table 8:(57) Risk stratification in pediatric ALL	
High Risk (HR)	• Poor Prednisolone Response (PPR) • No Complete Remission (CR) on day 33 • t (9; 22) ; t (4; 11) .
Medium Risk (MR)	• No HR criteria • Initial $\geq 20 \times 10^9$/L • Age at diagnosis < 1 or > 6 years • T -Acute Lymphoblastic Leukemia
Standard Risk (SR)	• No HR criteria, and • Initial WBC $\leq 20 \times 10^9$/L, and • Age at diagnosis between 1 - 6 years

Note: CNS status was not a stratification criterion

Treatment of pediatric ALL (≥1 < 15 years**)**

The basic BFM structure involves: 1) an induction regime consisting of oral corticosteroids, intravenous vincristine along with daunorubicin, intramuscular L-asparaginase, and intrathecal cytarabine with methotrexate; 2) a consolidation regime with 6-mercaptopurine and intravenous and intrathecal methotrexate; 3) a re-intensification regime with dexamethasone, vincristine, doxorubicin, and L-asparaginase followed by cyclophosphamide, cytarabine, 6-thioguanine, and intrathecal methotrexate; and 4) maintenance therapy with oral methotrexate and 6-mercaptopurine for a maximum time of 24 to 36 months .(67, 68)

Later, as stated by Smith et al.,(69) treatment modifications tested in inter group trials identified several key points: the inclusion of an interim maintenance phase, augmentation of BFM-type delayed intensification, and minimizing the use of cranial irradiation for CNS prophylaxis in children. These approaches, which are focused on prolonged and intensive use of the "pivotal" drugs glucocorticoids, vincristine, l-asparaginase (and lately, use of an extended release PEG-asparaginase,(70) methotrexate, and anti- metabolites), have improved the cure rates in a large number of children with ALL.

Thus, the BFM protocol has evolved through multiple sequential trials with an aim of maintaining high remission rates along with minimizing the long-term toxicity. The present cure rates in children with the BFM 95 protocols have approached 80 % from the initial 50 % with a reduction in the long term toxicity.(5)

Data from the developing countries on the use of the pediatric BFM ALL protocols is scarce, though the results of the BFM 76/79 ALL protocol over the years from 1985 to 2003 in

the Indian population < 15 years have been published. The estimated Kaplan Meier estimate 5 year OS, EFS and DFS was 59.8%, 56%, and 53.9%, respectively.(16)

[IV] Evaluation of MRD (Minimal Residual Disease):

A significant cause of treatment failure in ALL has traditionally been due to relapse of the disease.(1) in any treatment regimen it is vital to identify early those patients who do not achieve remission in order to achieve a better cure. Among the primary prognostic factors, an early response to the therapy has traditionally been considered as a significant factor for survival.(1, 71) Establishing the role of the minimal residual disease in delivering a risk based approach to the therapy has been one of the major challenges in the last decade or so.

Patients with acute leukemia may have a total of approximately 10^{12} malignant cells at the time of their diagnosis.(72,73) Though, a state of complete remission is considered to be when fewer than 5% of the cells in bone marrow (BM) sample are morphologically identifiable blasts, a significant tumor cells close to 10^{11} may not be detected on morphology alone.(74) These persistent tumor cells, not detected by morphology, defines a state of minimal residual disease.(75)

These blast cells can be recognized either by either

(i) Clonal rearrangement of immunoglobulin and T-cell receptor genes,

(ii) Expression of gene fusions, and /or

(iii) Leukemia-associated specific Immunophenotype.

ALL cells express immunophenotypic features that can be used to distinguish them from normal hematopoietic cells, including hematogones and activated lymphocytes. (76) During the last decade, levels of minimal residual disease measured either quantitatively by the use of PCR based techniques or by flow cytometry, have been successfully used to predict the prognosis, irrespective of the historically proven risk factors, like age and WBC count at presentation.(77–79) Majority of cells in approximately 95% of cases express immunophenotype, which are quite dissimilar from those of normal cells thereby allowing a sensitivity of detection of 0.01%. (80,81) MRD based risk stratification and the subsequent risk directed therapy will be the new standard of care in the coming years.(82, 83)

Molecular detection of MRD has established.(84) Flow cytometry (FCM), although less standardized, is quicker, generally cost effective and more informative (64,85,86). In a study by Helene Cave et al, it was shown that the relative risk of relapse at end of induction was found to be higher in patients with persistent disease than those without any disease. On comparison, chances of developing a relapse was significantly higher in patients with detectable disease than without detectable disease (87) Thus, it's important to identify prognostic factors signifying relapse early in any protocol, in order to justify a therapeutic change. MRD as a significant prognostic marker has already been incorporated in the newer BFM protocols like the BFM 2000 and the IC BFM 2002. Recently, flow cytometry to identify MRD for B cell ALL has been standardized and reported from our institute.(88) In present study, we will validate same by comparing the clinical outcome of the MRD negative verses those who are MRD positive.

Aims and Objectives

1. To study the clinical profile of children and adults diagnosed with acute lymphoblastic leukemia in our institute and their treatment outcome, when treated with different BFM protocols over the years.
2. To evaluate the clinical outcome in adolescent patients with acute lymphoblastic leukemia between 15 - 20 years of age, by using pediatric treatment regimens instead of adult regimens as currently used.
3. To assess the role of minimal residual disease monitoring by flow cytometry at time of documenting remission, post induction phase of chemotherapy.

Patients and Methods:

Our Institutional Review Board (IRB) approved this study.

This is a combined descriptive and prospective analysis of newly diagnosed patients with acute lymphoblastic leukemia (ALL) diagnosed in the department of hematology at Christian medical college, Vellore.

Duration of the study: 1st of July 2012 till 28th of February 2014.

Definitions:

Diagnosis- The diagnosis of acute lymphoblastic leukemia was made according to the WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues Fourth Edition.

The presence of ≥ 20% blasts was mandatory either in the peripheral blood or on the bone marrow. The presence of < 20 % blasts was acceptable only in those with recurrent genetic abnormalities.

Detailed definitions are as shown in table 9 below.

Table 9: (5, 89) Definitions used in the study	
Treatment response	
Prednisolone response (PR)	Determined after 7 days of monotherapy with prednisone and one IT dose of MTX on day 1 Presence of < 1000 blasts in peripheral blood on day 8 was defined as Poor PR and ≥1000/ ml blasts as Good PR
Complete remission	Defined as < 5% blasts in the regenerating BM, absence of leukemic blasts in blood and CSF, and no evidence of localized disease.
Treatment outcome	
End induction failure	Defined as not having achieved CR after the initial induction chemotherapy.
Relapse	Defined as recurrence of X25% lymphoblasts in BM and/or localized leukemic infiltrates at any site.
▪ Very early relapse	Relapse within 18 months of the initial therapy
▪ Earrly relapse	Relapse > 18 months from initial therapy and < 6 months after cessation of frontline therapy
▪ Late	Relapse after 6 months of frontline therapy
Survival definitions	
Overall survival	Defined for all patients; measured from the date of diagnosis to the date of death from any cause.
Event free survival	Defined for all patients; measured from the date of diagnosis to relapse from CR or death from any cause. If patient has relapsed and died, relapse is taken as an event.

Participants:

All patients seen and diagnosed as having acute lymphoblastic leukaemia in the department of haematology will be eligible for this study. They will be enrolled after getting written informed consents and where applicable assent forms.

Variables:

Objective 1: The data analysis for the adult ≥ 15 years with acute lymphoblastic leukaemia will be a retrospective and a descriptive study. This will be done by retrieval of the records from 2004 till 2012 and their data will be analysed to assess the effectiveness of the currently used adult GMALL (modified BFM) protocol for any future changes.

Appendix – Protocol attached.

1] (Modified BFM) Adult GMALL

Objective 2: There has been a change in the protocol design of the pediatric population diagnosed with acute lymphoblastic leukaemia from 2008 in our department. For patients with resources, the protocol has been changed to a BFM 95 regimen to improve their response rates and reduce their long-term toxicity. The present study is thus a retrospective as well as a prospective attempt to assess the response rates and assess the results of the BFM ALL 95 involving children < 15 years of age being treated in our institute from 2008 to February 2014. These results will be compared to non BFM 95 protocols being currently used in our department.

Appendix - Protocols attached:

2a] Intermediate risk BFM 95 (private ward)

2b] Intermediate risk (Radiotherapy based protocol) (General ward)

3] Standard risk BFM 95

4] Standard risk (Non Methotrexate/Non radiotherapy based study protocol)

Objective 3: Adolescents (≥ 15 ≤ 20 years) have so far being treated with the adult based modified GMALL regimens and their results from our institute have been published. The 5 year EFS was 46.7 %. By using established paediatric regimen, like the intermediate risk BFM 95, we aim to improve this response rates to approximately 60%. We anticipate at least 50 adolescents to be treated between the mentioned study period of May 2012 to February 2014.

Appendix – Protocol attached.

2a] Intermediate risk BFM 95 (private ward)

2b] Intermediate risk (Radiotherapy based protocol) (General ward)

Objective 4: The MRD study will be a prospective study and will include children and adults being treated in the department of haematology, who will undergo testing for the minimal residual disease by flow cytometry, by characterizing the leukaemia associated immunophenotype (LAIP) at diagnosis, using a combination of 6 tubes containing different

antibody combinations, which have recently been standardized in our department. We plan to do this analysis for a total of 100 cases initially. MRD assessment via flow has recently been standardized study in our department.(88) The outcome will be compared between the patients who are MRD negative versus those who are MRD positive.(90)

The following recently standardized antibody combinations will be used.(88)

	FITC	**PE**	**PerCp**	**APC**
Tube 1	CD20	CD10	CD45 PerCP	CD19
Tube 2	CD22	CD34	CD45 PerCP	CD19
Tube 3	CD38	CD10	CD34 PerCP-cy5.5	CD19
Tube 4	CD11a	CD10	CD45 PerCP	CD19
Tube 5	CD 38	CD 10	CD 34 PerCP-cy5.5	CD 19
Tube 6	CD123	CD 10	CD 34 PerCP-cy5.5	CD 19

Fluor chromes:

- FITC: Fluorescein isothiocyanate
- PE: Phycoerythrin
- PerCp: Peridinin- chlorophyll -protein complex
- APC: Allophycocyanin

Data Sources/measurement: Clinical data will be retrieved from the outpatient and in-patient records in the case of historical data. For prospective cases enrolled on this study the data will be collected and recorded in real time.

Bias: Since all consecutive patients with newly diagnosed ALL will be enrolled in this study, we do not anticipate any bias in our study.

Statistical methods: The adult data analysis is only a descriptive study as there is no change in the protocol, which was used earlier. The adolescent study group will be a prospective study to see the outcome of paediatric regimens in this age group. The data derived from the paediatric patients will be compared with non BFM 95 regimens being used previously and the changes will be reported. Any significant variable will also be reported. The MRD study is an exploratory study to assess its role as a stratification criterion.

Descriptive statistics were calculated for all variables. Differences in proportions were assessed using the $\chi 2$ or Fisher exact statistic. Differences in means were tested using a Mann-Whitney-U test or t-test as appropriate. The probability of survival we estimated with the use of the product-limit method of Kaplan and Meier for overall survival and event-free survival and compared by the log-rank test. All survival estimates are reported ± 1 SE. The relationships of clinical features to outcome were analyzed by Cox proportional hazard model. All P values were 2-sided, with values of .05 or less indicating statistical significance. Statistical analysis was performed using SPSS 16.0 software (SPSS, Chicago, IL).

Results

Figure 1: Age distribution of acute lymphoblastic leukemia (Jan 2004- Feb 2014)

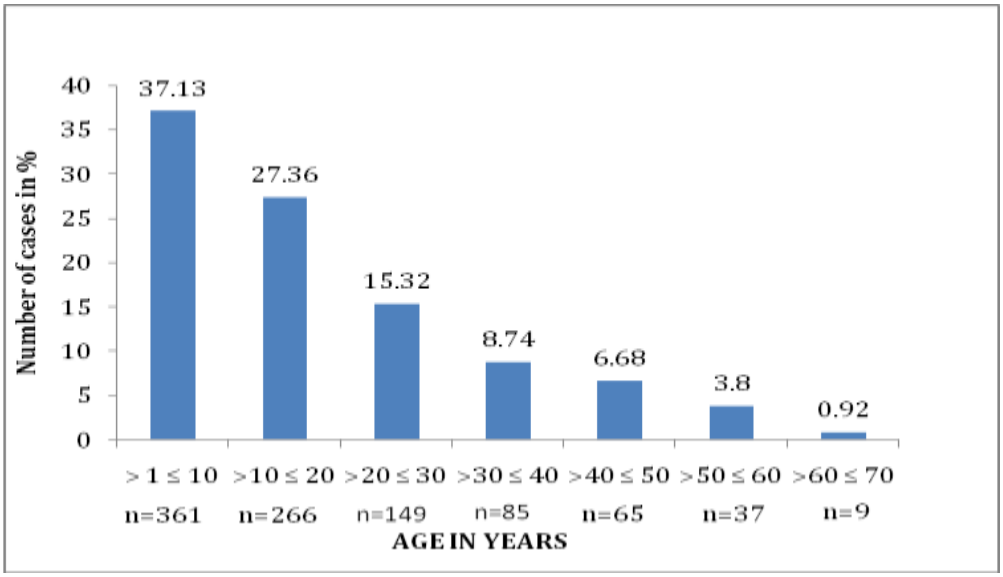
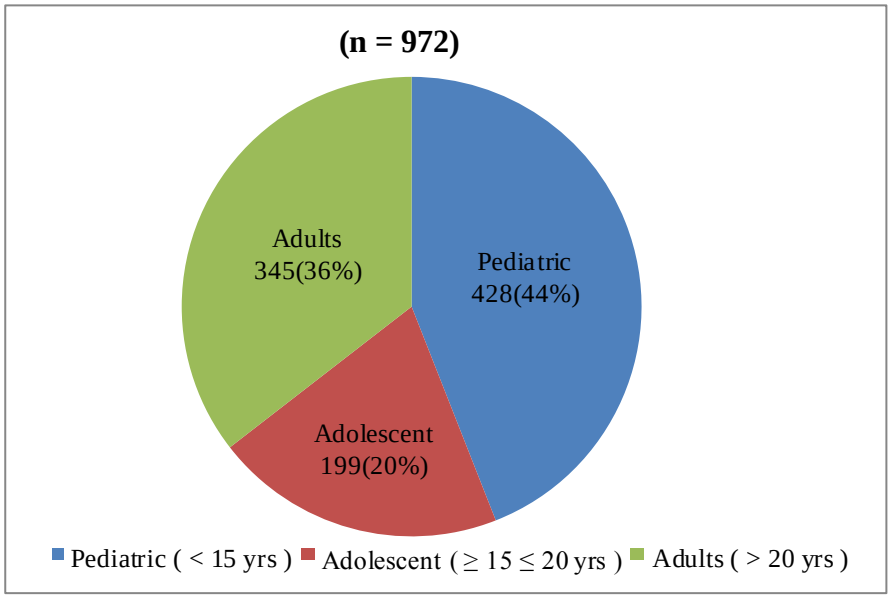


Figure 2: Age based statistics (Jan 2004-Feb 2014)



Objective 1: Adult descriptive study

A retrospective and a prospective study

Table 1: Study period and number of cases	
Study duration	**N**
Jan 2004 – June 2012 (> 15 years)	**392**
July 2012 – Feb 2014 (> 20 years)	**63**
Total cases analyzed	**455**

Table 2: Baseline characteristics	
Variables	**Adult GMALL Group n (%) / Median (range) (n – 455)**
Age (years)	26 (15-67)
Sex (male)	321 (70.5)
Physical findings : • Hepatomegaly (cm)	3 (1 -20)
• Splenomegaly (cm)	3 (1 -15)
• CNS Disease (%)	64 (14.1)
• Pleural Effusion (%)	18 (4.0)
• Mediastinal mass (%)	34 (7.5)
• Testicular mass (%)	2 (0.6)
Lab Parameters : • WBC (x 10^9 / Lt)	9.5 (0.3 – 531.4)

Table 3: Immunophenotyping, cytogenetics and molecular genetics	
Variables	**Adult GMALL Group n (%) / Median (range) n – 455**
IPT : n	447 (98.2)
▪ B cell	333 (73.2)
▪ T cell	114 (25.1)
Cytogenetics® n	404 (88.7)
▪ Standard	301 (74.6)
▪ Poor	103 (25.5)
RT PCR : n	348 (76.5)
▪ B ALL	319 (91.6)
▪ T ALL	29 (8.3)
B cell	
▪ BCR ABL1	60 (18.8)
▪ TEL AML	6 (1.8)
▪ MLL	4 (1.2)
▪ E2A PBX	14 (4.3)
▪ None of the above	235 (76.3)

Cytogenetic risk stratification: (91)

a. **Poor risk** – **(i)** t (9:22), (**ii)** t (4:11), (**iii)** Complex karyotype, **(iv)** iAmp 21, **(v)** Low hypodiploidy/near triploidy, **(vi)** t (17:19).

b. **Standard risk** - All others including normal karyotype.

Table 4: Risk status and treatment response	
Variables	**Adult GMALL Group n (%) / Median (range) n – 455**
Overall risk: ®	
▪ SR	331 (72.7)
▪ HR	124 (27.2)
Treatment taken n	455 (100)
Prednisolone response (PR) assessed	314 (69)
▪ **Good PR**	260 (82.8)
▪ **Poor prednisolone response**	54 (17.2)
Prednisolone response not assessed	141 (30.9)

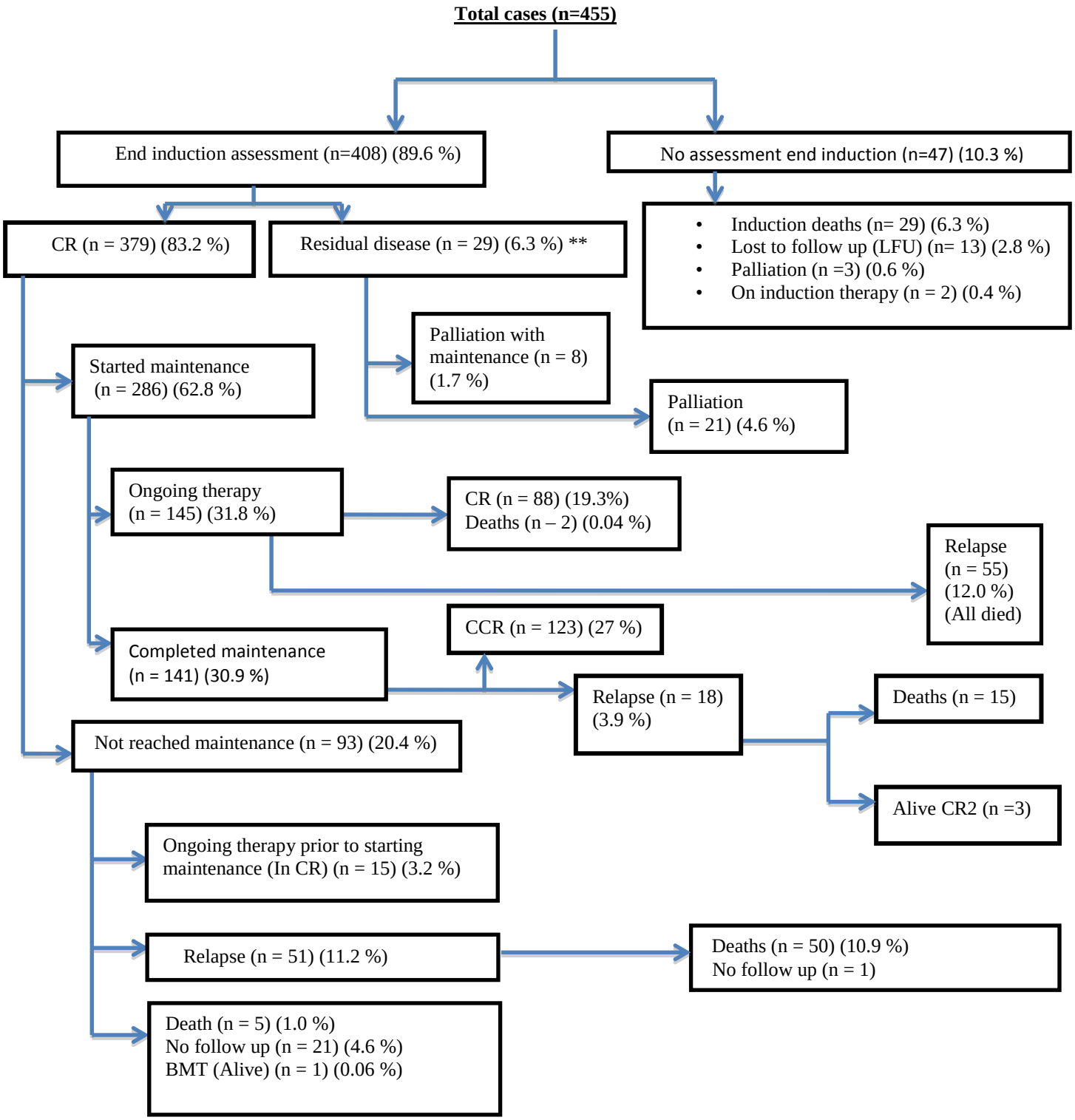
® Overall risk stratification in adult acute lymphoblastic leukemia:

Standard risk - (**i)** Good prednisolone response,
(ii) Absence of t (9:22) and t (4:11)
(iii) End induction remission.

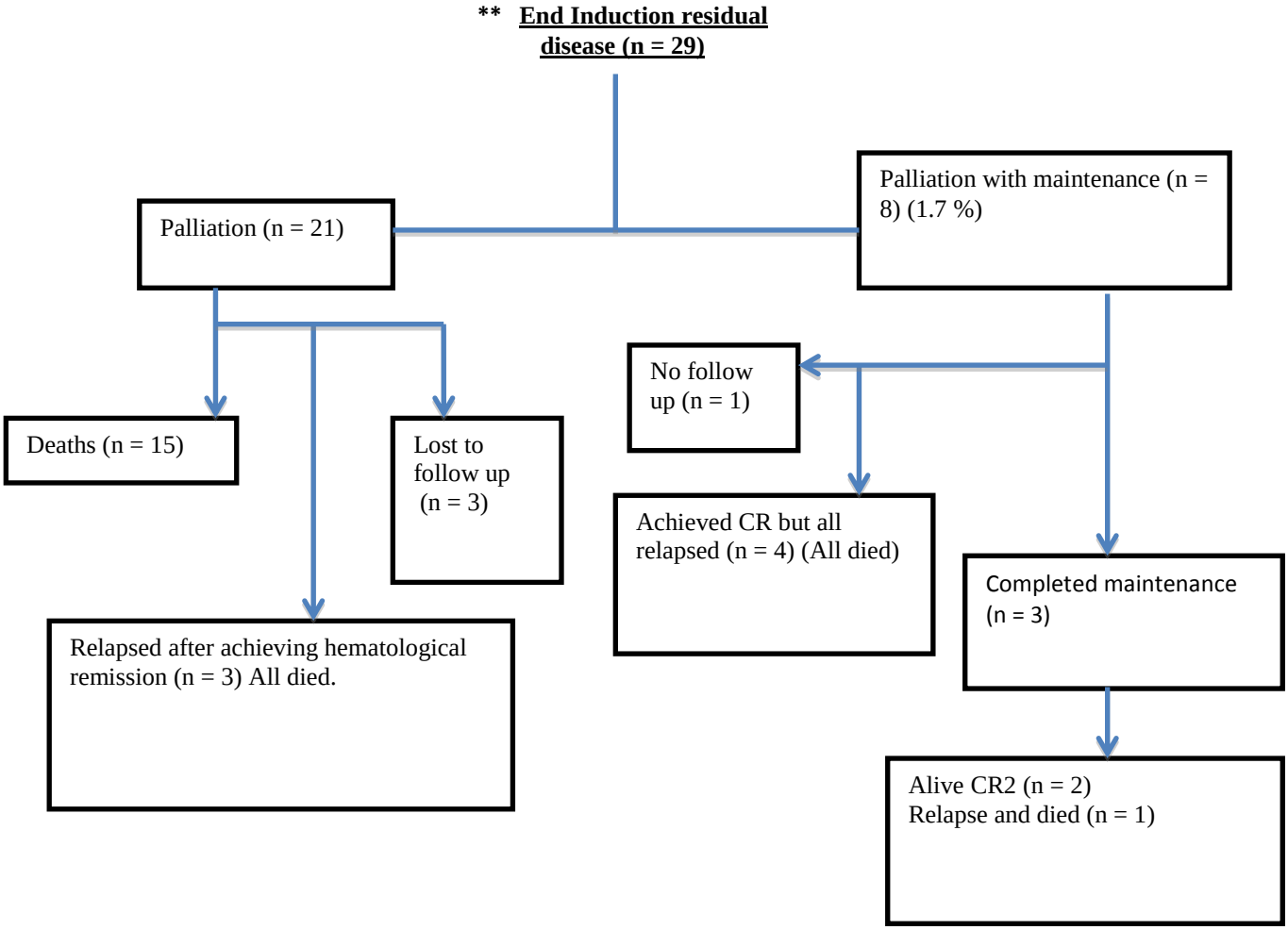
High risk - **(i)** Poor prednisolone response,
(ii) Presence of t (9:22) and t (4:11)
(**iii)** End induction failure.

Table 5: Follow up of outcome	
Variables	**Adult GMALL Group** **n (%) / Median (range)** **n = 455**
Relapse	132 (29.0)
• Very Early	93 (20.4)
• Early	21 (4.6)
• Late	18 (4.0)
Total Deaths	179 (39.3)
• Progressive disease	140 (78.2)
• Infection	39 (21.8)
Current status	
Alive	276 (60.7)
Completed therapy in CCR (Continuous complete remission)	123 (27)
On treatment in CR (Complete remission)	103 (22.6)
5 year EFS	50.1 ± 2.9 %
5 year OS	51.6 ± 2.9 %
Median Follow up	65 months

Adult acute lymphoblastic leukemia flow chart (Jan 2004 to Feb 2014)
(Flow chart 1)



Adult acute lymphoblastic leukemia flow chart (Jan 2004 to Feb 2014) (Flow chart 2)



Survival statistics: (Figures 3a and 3b)

The event free survival (EFS) and the overall survival (OS) were calculated using the Kaplan- Meier estimates.

OS in adult acute lymphoblastic leukemia: (figure 3a)

At the time of this analysis, the 5 year overall survival of the entire adult cohort (n = 455) was 51.6 ± 2.9 % with a median follow up of 65 months.

For OS, death due to any cause was considered as an event. For the purpose of this analysis, patients who had relapsed during therapy and then subsequently lost to follow up were considered as dead, 30 days after the last follow up.

EFS in adult acute lymphoblastic leukemia: (figure 3b)

An event was considered whenever there was a relapse or death. In cases where death was secondary to relapse and progressive disease, the date of relapse was considered an event in that patient.

At the time of this analysis, the 5 year event free survival of the entire adult cohort (n = 455) was 50.1 ± 2.9 % with a median follow up of 65 months.

Figure 3a: Overall survival

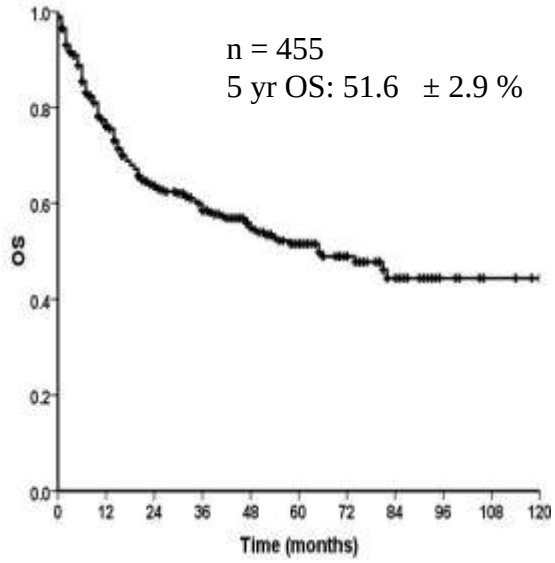


Figure 3b: Event free survival

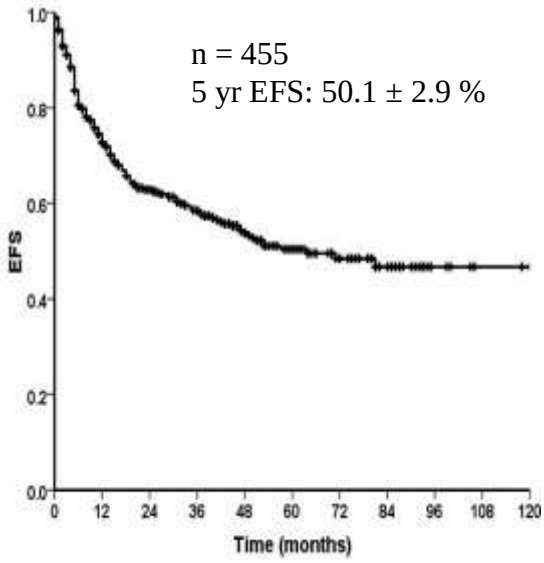


Figure 3a**:** Kaplan Meier curve for overall survival of adults (≥ 15 years) with acute lymphoblastic leukemia (n = 455).
With a median follow up period of 65 months, the five year survival was 51.6 ± 2.9 %.

Figure 3b: Kaplan Meier curve for event free survival of adults (≥ 15 years) with acute lymphoblastic leukemia (n = 455).
With a median follow up period of 65 months, the five year survival was 50.1 ± 2.9 %.

Objective 2a results:

Standard risk acute lymphoblastic leukemia (SR ALL):

Table 6: Standard risk inclusion criteria : (Jan 2008 to Feb 2014)

Variables	Study protocol Non Methotrexate / Non Radiation based chemotherapy	BFM 95 Methotrexate based Chemotherapy
Age (years)	> 1 < 6	> 1 < 6
Total count (per cmm)	< 20,000	< 20,000
Prednisolone response	Good Prednisolone response	Good Prednisolone response
High risk cytogenetics	t (9:22), t (4:11) are excluded	t (9:22), t (4:11) are excluded
Immunophenotype	No T cell	No T cell
Myeloid markers	Not a criteria	No myeloid markers
CNS / Testis involvement	Not a criteria	Not a criteria

Since 2008, 67 children with acute lymphoblastic leukemia have been stratified into the standard risk category. Out of these, 23 children opted for the medium dose methotrexate (MTx) based therapy of BFM 95 protocol and 44 children opted for the non-methotrexate / non-radiotherapy (study protocol) based chemotherapy.

Table 7: Baseline characteristics			
Variables	**SR (Study protocol) n (%) / Median (range) (n = 44)**	**SR (BFM 95) n (%) / Median (range) (n = 23)**	**P value**
Age (years)	4 (2 – 6)	3 (1 – 6)	0.645
Sex (male)	30 (68.2)	13 (56.5)	0.424
Physical findings : • Hepatomegaly (cm)	3 (1 – 5)	2 (1 – 5)	0.678
• Splenomegaly (cm)	2 (1 – 6)	2 (1 – 3)	0.631
• CNS Disease (%)	0	1 (4.3)	0.343
• Pleural Effusion (%)	0	0	-
• Mediastinal mass (%)	0	0	-
• Testicular mass (%)	0	0	-
Lab Parameters : • WBC (10^9 / Lt)	5.5 (1.5 – 18.3)	5.8 (1.8 – 13.8)	0.505

There was no statistically significant difference between the two groups in their baseline characteristics

Table 8: Cytogenetics, molecular genetics and risk status

Variables	SR (Study protocol) n (%) / Median (range) (n = 44)	SR (BFM 95) n (%) / Median (range) (n = 23)	P value
Cytogenetics :**	41 (93.1)	21 (91.3)	0.438
▪ Favourable	28 (68.3)	15 (71.4)	
▪ Intermediate	10 (24.3)	6 (28.6)	
▪ Poor	3 (7.3)	-	
RT PCR :	43 (97.7)	22 (95.7)	1.000
▪ BCR ABL	-	-	-
▪ TEL AML	5 (11.4)	4 (17.3)	0.467
▪ MLL	-	-	-
▪ E2A PBX	-	-	-
▪ No result	38(88.3)	18(81.8)	1.000

** **Cytogenetic risk stratification: (92)**

a. **Favourable risk: (i)** Hyperdiploidy

b. **Poor risk:** **(i)** t (9:22), (**ii)** t (4:11), (**iii)** Complex karyotype, (**iv)** iAmp 21, **(v)** Low hypodiploidy/near triploidy **(vi)** t (17:19).

c. **Intermediate risk** - All others, including normal karyotype.

There was no statistically significant difference between the two groups in their baseline laboratory features.

Table 9: Treatment response			
Variables	**SR (Study protocol) n (%) / Median (range) (n = 44)**	**SR (BFM 95) n (%) / Median (range) (n = 23)**	**P value**
Protocols			
▪ SR MD MTx	-	23	-
▪ SR (No MTX/ No RT)	44	-	
Prednisolone Response (PR): N	28 (63.6)	13 (56.5)	
▪ GPR (Good)	28 (100)	13(100)	1.000
End Induction Remission status	42 (95.4)	23 (100)	1.000
▪ CR (Complete remission)	42 (100)	23 (100)	
End Induction Not assessed	2 (4.5)	-	-
▪ Induction deaths	0(0)	0(0)	-
▪ Ongoing treatment Induction phase	2 (4.5)	-	-
Received maintenance therapy:			
Yes	35 (87.5)	21 (91.3)	0.154
No	9 (20.4)	2 (8.6)	
• Pre maintenance phase	4(44.4)	2(100)	
• Relapse	1(11.1)	0(0)	-
• No follow up	4(44.4)	0(0)	-

Table 10: Follow up of outcome			
Variables	**SR (Study protocol) n (%) / Median (range) (n = 44)**	**SR (BFM 95) n (%) / Median (range) (n = 23)**	**P value**
Relapse	7 (15.9)	1 (4.3)	0.247
▪ Very early	2 (4.5)	1 (4.3)	0.416
▪ Early	2 (4.5)	-	-
▪ Late	3 (6.8)	-	
Total Deaths	4 (9.1)	1 (4.3)	**1.000**
Cause of death			
• Progressive disease	4 (100)	1 (100)	
• Infection	-	-	-
Current status			
CR – Completed treatment	**16 (36.3)**	5 (21.7)	0.342
CR – On Treatment	**21 (47.7)**	17 (73.9)	0.072
Induction deaths	-	-	-
OS Alive	40 (90.9)	22 (95.6)	0.483

There was a higher incidence of relapse seen in the children treated with the study protocol in comparison to those treated with the BFM 95 protocol, though the actuarial median follow up was shorter in the children treated with the BFM 95 protocol.

Survival statistics: (Figures 4a – 4b)

The overall survival (OS) and the event free survival (EFS) were calculated using the Kaplan- Meier estimates.

OS in standard risk acute lymphoblastic leukemia: (Figure 4a)

At the time of this analysis, the 3 year overall survival of the BFM 95 based cohort (n = 23) was 95 ± 4.9 % with an actuarial median follow up of 25 (1.5 - 65) months and 3 year overall survival of the non methotrexate/non radiation based study protocol was 90.1 ± 5.6 % with an actuarial median follow up of 27 months (1.5 - 68) months. For the purpose of this analysis, patients who had relapsed during therapy and then subsequently lost to follow up were considered as dead, 30 days after the last follow up.

A log rank comparison among those treated with the BFM 95 and the non methotrexate/non radiation based study protocol did not show a statistically significant survival difference. (P = 0.752).

EFS in standard risk acute lymphoblastic leukemia: (Figure 4b)

At the time of this analysis, the 3 year event free survival of the BFM 95 based cohort (n = 23) was 95 ± 4.9 % with an actuarial median follow up of 25 (1.5 – 65) months. The 3-year event free survival for the non methotrexate/non radiation (study protocol) based cohort was 86.5 ± 6.5 % with an actuarial median follow up of 17 (1 - 64) months. There was no significant statistical difference between the two cohorts. An event was considered whenever

there was a relapse or death. In cases where death was secondary to relapse and progressive disease, the date of relapse was considered an event in that patient.

A log rank comparison among those treated with the BFM 95 and the non methotrexate/non radiation based study protocol did not show a statistically significant survival difference ($p = 0.391$).

Figure 4a: Overall survival **Figure 4b: Event free survival**

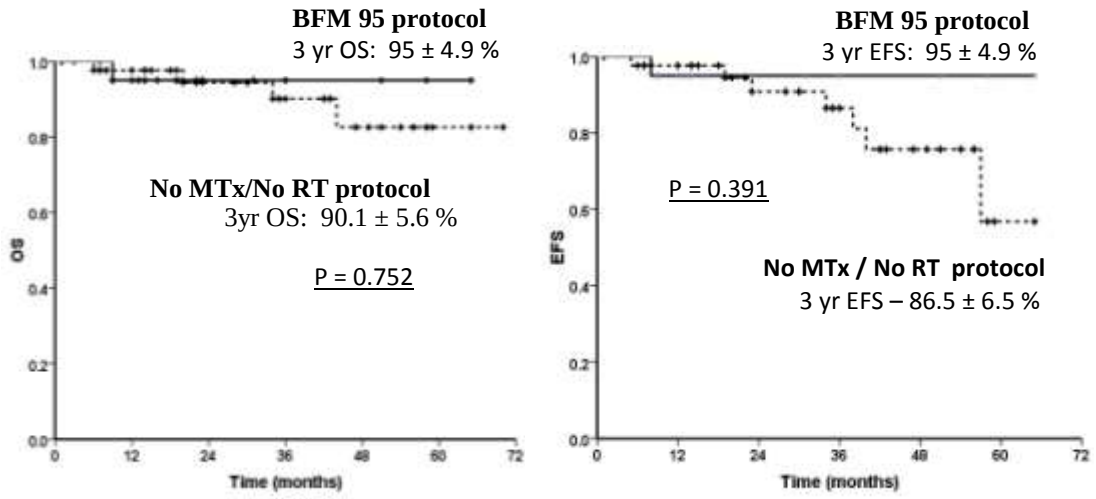


Figure 4a: Kaplan Meier curves for overall survival (OS) in children (>1 < 6 years) with standard risk B cell acute lymphoblastic leukemia treated with BFM-95 protocol (n =23) and the non methotrexate/non radiation based study protocol ((n = 44).
With an actuarial median follow up period of 25(1.5 - 65) months and 27(1.5 - 68) for those treated with the BFM 95 protocol and those with the Non MTx/Non RT based study protocol; the three year overall survival was 95 ± 4.9 % and 90.1 ± 5.6 % respectively. (*P* value= 0.752)

Figure 4b: Kaplan Meier curves for event free survival (EFS) in children (>1 < 6 years) with standard risk B cell acute lymphoblastic leukemia treated with BFM-95 protocol (n = 23) and the non methotrexate/non radiation based study protocol (n = 44).
With an actuarial median follow up period of 25(1.5 - 65) months and 17(1- 64) months for those treated with the BFM 95 protocol and those with the Non MTx/Non RT based study protocol; the three year event free survival was 95 ± 4.9 % and 86.5 ± 6.5 % respectively. (*P* value= 0.391)

Objective 2b

[II] Intermediate risk acute lymphoblastic leukemia (IR- ALL)

Table 11: Inclusion criteria of intermediate risk group **Jan 2004 to Feb 2014 – Radiation based protocol (Non methotrexate)** **Jan 2008 to Feb 2014 – BFM 95 (Methotrexate based) protocol**	
Variables	
Age (years)	> 1 < 15
Total count (per cmm)	> 20,000
Prednisolone response (PR)	Good
Immunophenotype	T cell
High risk cytogenetics	Absent

Note:

Additional criteria for stratification into Intermediate risk in the non methotrexate/ non radiation based protocol

i. B cell ALL with presence of two myeloid markers on immunophenotype.
ii. B cell ALL with CNS Disease.
iii. B cell ALL with testicular disease.

Since 2004, 285 children with acute lymphoblastic leukemia have been stratified into the intermediate risk category. 251 children opted for the non-methotrexate / radiotherapy based chemotherapy, which was unchanged since 2004. Beginning from July 2012, 34 children opted for the methotrexate based therapy of intermediate risk BFM 95 protocol.

Table 12a: Baseline characteristics of intermediate risk group			
Variables	**BFM 95 based n (%) / Median (range) (n – 34)**	**RT based n (%) / Median (range) (n – 251)**	**P value**
Age (years)	7 (1 -14)	6 (1 -14)	0.988
Sex (male)	25 (73.5)	164(65.3)	0.440
Physical findings : ▪ Hepatomegaly (cm)	2 (1 – 6)	3 (1 -12)	**0.017**
▪ Splenomegaly (cm)	2 (1 -11)	2 (1-16)	0.930
▪ CNS Disease (%)	3 (8.8)	34 (13.5)	0.591
▪ Pleural Effusion (%)	1 (2.9)	3(1.2)	0.400
▪ Mediastinal mass (%)	-	12 (4.8)	0.372
▪ Testicular mass (%)	1(3.8)	2(1.2)	0.349
Lab Parameters : WBC (10^9 / Lt)	16.7 (1.5 – 445.2)	21.3 (0.2 – 539.4)	0.542

Except a higher median size of liver, there was no significant difference between the two groups in terms of their baseline demographics.

Table 12 b: Immunophenotype, cytogenetics and molecular genetics			
Variables	**BFM 95 based n (%) / Median (range) (n – 34)**	**RT Based n (%) / Median (range) (n – 251)**	**P value**
IPT : B cell	27 (79.4)	205 (81.6)	0.338
T cell	5 (14.7)	42 (16.7)	
Cytogenetics : n	32 (94.1)	220 (87.6)	0.013
▪ Favourable	17 (53.1)	61 (27.7)	
▪ Intermediate	12 (37.4)	115 (52.3)	
▪ Poor	3 (9.4)	44 (20)	
RT PCR : n	28 (82.4)	220 (87.6)	0.414
▪ B ALL	27 (96)	197 (90)	0.267
▪ T ALL	1 (4)	22 (10)	
B ALL			-
▪ BCR ABL	-	14 (7.1)	0.383
▪ TEL AML	3 (11)	30 (15)	0.778
▪ MLL	-	1 (0.5)	1.000
▪ E2A PBX	1 (4)	12 (6)	1.000
▪ **No result**	23(85.1)	140 (73.6)	-

** **Cytogenetic risk stratification: (92)**

a. **Favourable risk: (i)** Hyperdiploidy

b. **Poor risk:** **(i)** t (9:22), (**ii)** t (4:11), (**iii)** Complex karyotype, (**iv)** iAmp 21, **(v)** Low hypodiploidy/near triploidy **(vi)** t (17:19).

c. **Intermediate risk -** All others, including normal karyotype.

Table 13: Overall Risk status			
Variables	**BFM 95 based n (%) / Median (range) (n – 34)**	**RT Based n (%) / Median (range) (n – 251)**	**P value**
Overall Risk			-
▪ IR	33 (97.1)	209 (83.2)	0.039
▪ HR*	1 (2.9)**	42 (16.7)***	

* **HR (High risk)**: **(i) Poor prednisolone response**

(ii) End Induction failure

(iii) High risk cytogenetics – t (9:22), t (4:11)

** In the methotrexate based treatment arm of BFM 95, there was one patient who had a residual disease at the end of induction and was subsequently categorized into high risk.

*** In the radiotherapy based treatment arm, there were 42 (16.7 %) patients who were later stratified as high risk due to either a poor prednisolone response or philadelphia positivity, but continued to be treated with the intermediate risk protocol due to insufficient finances required for a high risk protocol and a transplant. Overall, there were a significant number of high risk cases who were treated with the radiotherapy based protocol in comparison to the methotrexate (BFM 95) based treatment regimens.

Table 14: Treatment response

Variables	BFM 95 based n (%) / Median (range) n – 34	RT based n (%) / Median (range) n – 251	P value
Protocols :			-
MD MTx (2gms/m^2)	29 (85.3)	-	-
HD MTx (5gms/m^2)	5 (14.7)	-	-
IR RT/No MTx	-	251 (100)	-
Prednisolone Response (PR):	24 (70.5)	182 (73)	-
▪ GPR (Good)	24 (100)	153 (84.1)	**0.030**
▪ PPR (Poor)	-	29 (15.9)	
End Induction status :	34 (100)	240 (95.6)	**1.000**
▪ CR (Complete remission)	33 (97.1)	231 (96.2)	0.782
▪ RD (Residual disease)	1 (2.9)	9 (3.7)	
No end Induction BM	-	11 (4.3)	-
• Induction deaths	-	6	-
• Lost to follow up	-	5	-
Received maintenance: Yes	26 (76.4)	194 (77.2)	0.915
No	8 (23.4)	57 (22.7)	
• Ongoing pre-maintenance	7(87.5)	18 (31.5)	-
• Deaths (Relapse + Infection)	1 (2.9)	17 (29.8)	-
• BMT	-	1 (1.7)	-
•No follow up	-	21 (36.8)	-

Table 15: Follow up of outcome of intermediate risk group			
Variables	**BFM 95 Based (< 15 yrs) n (%) / Median (range) n – 34**	**RT Based (< 15 yrs) n (%) / Median (range) n - 251**	**P value**
Relapse	-	48 (19.1)	0.002
▪ Very early	-	21 (8.3)	0.05
▪ Early	-	19 (7.6)	
▪ Late	-	8 (3.2)	
▪ No relapse	34(100)	203 (80.8)	
Total Deaths	1 (2.9)	47 (18.7)	0.917
• Progressive disease	1 (100)	40 (85.1)	
• Infection	-	5 (10.6)	
• CNS Bleed	-	2 (4.3)	
Current status			
CCR – (Continous complete remission post completion of treatment)	2 (5.8)	90 (35.8)	< 0.001
CR – On Treatment	31 (91.1)	96 (38.2)	<.0.001
Induction deaths	0	6 (2.3)	
OS Alive	33 (97.1)	204 (81.3)	**0.025**

There was no relapse seen in the BFM 95 treatment arm, though the period of follow up was short. In comparison, there were 48 children who relapsed in the radiotherapy based treatment regimens and this was statistically significant.

Survival statistics: **(Figures 5a - 5b)**

The overall survival (OS) and the event free survival (EFS) were calculated using the Kaplan- Meier estimates.

OS in intermediate risk acute lymphoblastic leukemia: **(Figure 5a)**

At the time of this analysis, the 2 year overall survival of the BFM 95 based cohort (n = 34) was 96.9 ± 3.1 % with an actuarial median follow up of 27 (1 - 47) months and 2 year overall survival of the radiotherapy based cohort was 87.9 ± 2.3 % with an actuarial median follow up of 35 (1 - 116) months**.** For the purpose of this analysis, patients who had relapsed during therapy and then subsequently lost to follow up were considered as dead, 30 days after the last follow up.

A log rank comparison among those treated with the BFM 95 and the radiation based study protocol did not show a statistically significant survival difference. (P = 0.163).

EFS in intermediate risk acute lymphoblastic leukemia: (Figure 5b)

At the time of this analysis, the 2 year event free survival of the BFM 95 based cohort (n = 34) was 96.9 ± 3.1 % with an actuarial median follow up of 27 (1 - 47) months. The 2-year event free survival for the radiotherapy based cohort was 85.6 ± 2.4 % with an actuarial median follow up of 18 (1 -116) months. There was no significant statistical difference between the two cohorts.

An event was considered whenever there was a relapse or death. In cases where death was secondary to relapse and progressive disease, the date of relapse was considered an event in that patient.

A log rank comparison among those treated with the BFM 95 and the radiation based study protocol did not show a statistically significant survival difference. ($P = 0.103$).

Figure 5a: Overall survival

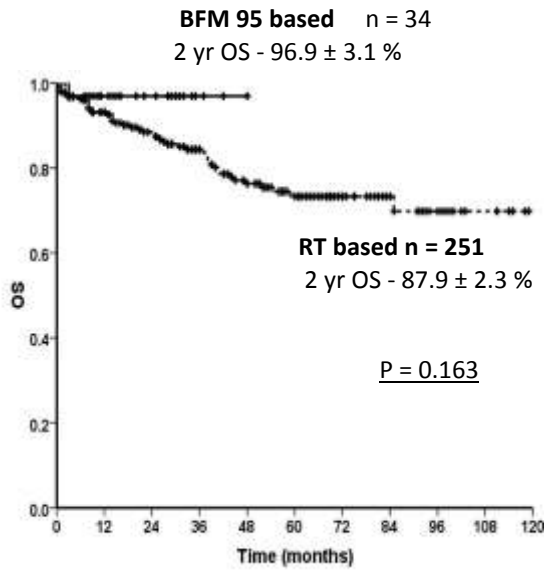


Figure 5b: Event free survival

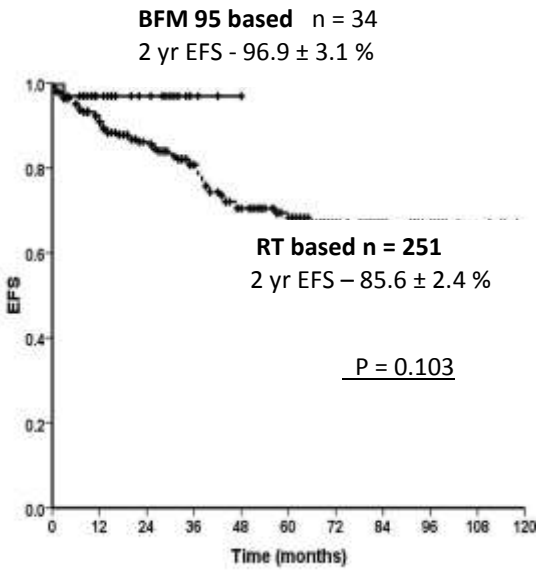


Figure 5a: Kaplan Meier curves for overall survival (OS) in children (>1 < 15 years) with intermediate risk acute lymphoblastic leukemia treated with BFM-95 protocol (n =34) and the Radiation based (RT) study protocol ((n = 251).
With an actuarial median follow up period of 27(1 - 47) months and 35(1-116) months for those treated with the BFM 95 protocol and those with the RT based study protocol; the three year overall survival was 96.9 ± 3.1 % and 87.9 ± 2.3 % respectively. (*P* value = 0.163)

Figure 5b: Kaplan Meier curves for event free survival (EFS) in children (>1 < 15 years) with intermediate risk acute lymphoblastic leukemia treated with BFM-95 protocol (n = 34) and the radiation based study protocol (n = 251).
With an actuarial median follow up period of 27 (1 - 47) months and 18 (1-116) months for those treated with the BFM 95 protocol and those with the radiation (RT) based protocol; the two year event free survival was 96.9 ± 3.1 % and 85.6 ± 2.4 % respectively. (*P* value = 0.103)

Objective 3:

A comparison of the clinical outcome in adolescents **(≥ 15 ≤ 20 yrs)** with acute lymphoblastic leukemia (ALL) treated with Intermediate risk pediatric-based regimens as against those treated with the adult GMALL regimens.

Since Jan 2004, 181 adolescents **(≥ 15 ≤ 20 yrs)** with ALL have been treated.

- **Jan 2004 to July 2012:** 150 adolescents treated with adult modified GMALL regimen.
- **July 2012**: 31 adolescents treated with Intermediate risk pediatric-based regimens

Table 16: Baseline characteristics

Variables	Adolescent ALL (≥15 ≤20 yrs) (Pediatric Protocols) n (%) / Median (range) (n – 31)	Adolescent ALL (≥15 ≤20 yrs) (Adult Protocols) n (%) / Median (range) (n – 150)	P value
Age (years)	17 (15 -20)	17 (15 -20)	0.692
Sex (male)	24 (77.4)	115 (76.7)	1.000
Physical findings : Hepatomegaly (cm)	4 (1-17)	3 (1 – 10)	0.451
Splenomegaly (cm)	6 (2 - 20)	3 (1 - 14)	0.009
CNS Disease (%)	7 (22.6)	22 (14.7)	0.286
Pleural Effusion (%)	1 (3.2)	5 (3.3)	1.000
Mediastinal mass (%)	0 (0%)	0 (0%)	0.215
Testicular mass (%)	1 (4.3)	0	0.167
Lab Parameters : WBC (10^9 / Lt)	24.1 (0.7 – 442.6)	9.75 (0.4 – 430.7)	0.082

Table 17: Immunophenotyping, cytogenetics and molecular genetics			
Variables	**Adolescent ALL (≥15 ≤20 yrs) (Pediatric Protocols) n (%) / Median (range) (n – 31)**	**Adolescent ALL (≥15 ≤20 yrs) (Adult Protocols) n (%) / Median (range) (n – 150)**	**P value**
IPT : B cell	**20 (64.5)**	110 (73.3)	0.502
T cell	11 (35.5)	38 (25.3)	
Cytogenetics : n	25 (80.6)	131 (87.3)	0.266
▪ Standard	18 (72)	107 (81.6)	
▪ Poor	7 (28)	24 (18.3)	
RT PCR : n	23(74.1)	115(76.6)	0.812
▪ T ALL	3(13)	13(11.3)	
▪ B ALL	20(86.9)	102(88.6)	
B ALL			
▪ BCR ABL	2 (10.0)	7 (6.8)	0.564
▪ TEL AML	-	4 (3.9)	
▪ MLL	-	-	
▪ E2A PBX	3 (15.0)	8 (7.8)	
▪ No result	15 (75)	83 (81.3)	

No significant difference between the two groups

Table 18: Risk status, treatment and response			
Variables	**Adolescent ALL (≥ 15 ≤ 20 yrs) (Pediatric Protocols) n (%) / Median (range) (n = 31)**	**Adolescent ALL (≥ 15 ≤ 20 yrs) (Adult Protocols) n (%) / Median (range) (n = 150)**	**P value**
Overall risk :	30*	150	0.262
▪ SR/IR	21(67.7)	119 (79.3)	
▪ HR	9 (30.0)	31 (20.6)	
Protocols :			-
IR MD MTx (2gms/m^2)	**9 (29.0)**	-	
IR HD MTx (5gms/m^2)	5 (16.1)	-	
IR RT/No HDMTx	17 (54.8)	-	
Modified GMALL	-	150 (100)	
Cranial RT **	23 **[IR RT protocol (B cell and T cell) = 17] + [IR MTx (T cell) = 6]**	150 (100)	**0.000**
Prednisolone response (PR): n	23 (74.1)	111 (74)	0.765
▪ GPR (Good)	20 (87)	92 (82.9)	
▪ PPR (Poor)	3 (13)	19 (17.1)	
PR not assessed	7(22.5)	39 (26)	

* One patient was not stratified due to insufficient data

** Indication of irradiation in pediatric protocol

(i) Adolescents (B cell and T cell) on Intermediate risk radiation based protocol
(ii) Adolescents with T - ALL on Intermediate risk Mtx based protocol
(iii) Adolescents with B - ALL with CNS III on Intermediate risk Mtx based protocol.

The only significant difference was a higher number of patients receiving cranial radiation in adolescents on the adult GMALL regimen.

Table 19: Follow up of outcome			
Variables	**Adolescent ALL (≥ 15 ≤ 20 yrs) (Pediatric Protocols) n (%) / Median (range) n = 31**	**Adolescent ALL (≥ 15 ≤ 20 yrs) (Adult Protocols) n (%) / Median (range) n = 15050)**	**P value**
End Induction Remission status : Assessed in	26 (83.8)	137 (91.3)	0.081
CR (Complete remission)	23 (74.1)	128 (85.3)	
RD (Residual disease)	3 (9.6)	9 (6.0)	
End induction not assessed	5 (16.1)	13 (8.6)	-
▪ Induction deaths	4 (80)	6 (46.1)	-
▪ Ongoing Induction	1 (20)	-	-
▪ No follow up	-	7 (53.8)	-
Received maintenance: Yes	15 (48.3)	111 (74.0)	0.599
No	16 (51.6)	39 (26)	
i. In pre-maintenance phase	9(56.2)	-	-
ii. Induction Deaths	4(25)	6(15.3)	
iii. Death due to relapse	-	21(53.8)	-
iv. Refractory disease	1(6.2)	-	-
v. No Follow up	2(12.5)	12(30.7)	
Relapse n	-	41 (27.3)	0.000
▪ Very early	-	31 (20.7)	0.012
▪ Early	-	6 (4.0)	
▪ Late	-	4 (2.7)	
Overall Alive patients	26 (83.8)	97 (64.6)	0.055
Continous complete remission (CCR)	-	53(35.3)	-
Complete remission (On treatment)	23(74.1)	38 (25.3)	-

A significantly higher relapse rate seen in adolescents treated with the adult GMALL regimens, but follow up was shorter in adolescents treated with pediatric regimens.

Survival statistics: **(Figures 6a - 6b)**

The overall survival (OS) and the event free survival (EFS) were calculated using the Kaplan- Meier estimates.

OS in intermediate risk acute lymphoblastic leukemia: **(Figure 6a)**

At the time of this analysis, the 1 year overall survival of the adolescents treated with intermediate risk pediatric protocol (n = 31) was 82.3 ± 7.3 % with an actuarial median follow up of 8 (1 - 19) months and 1 year overall survival of adolescents treated with the modified adult GMALL protocol was 81.4 ± 3.2 % with an actuarial median follow up of 27 months (1 - 118) months**.** For the purpose of this analysis, patients who had relapsed during therapy and then subsequently lost to follow up were considered as dead, 30 days after the last follow up.

A log rank comparison among those treated with the intermediate risk pediatric protocol and the modified adult GMALL protocol did not show a statistically significant survival difference. ($P = 0.996$).

EFS in intermediate risk acute lymphoblastic leukemia: (Figure 6b)

At the time of this analysis, the 1 year event free survival of the intermediate risk pediatric

protocol (n = 31) based cohort was 82.3 ± 7.3 % with an actuarial median follow up of 7.7 (1 - 19) months. The 1 year event free survival for the modified adult GMALL protocol based cohort was 75.9 ± 3.6 % with an actuarial median follow up of 18 (1 - 118) months. An event was considered whenever there was a relapse or death. In cases where death was secondary to relapse and progressive disease, the date of relapse was considered an event in that patient.

A log rank comparison among those treated with the intermediate risk pediatric protocol and the modified adult GMALL protocol did not show a statistically significant survival difference. (P = 0.752).

Figure 6a: Overall survival

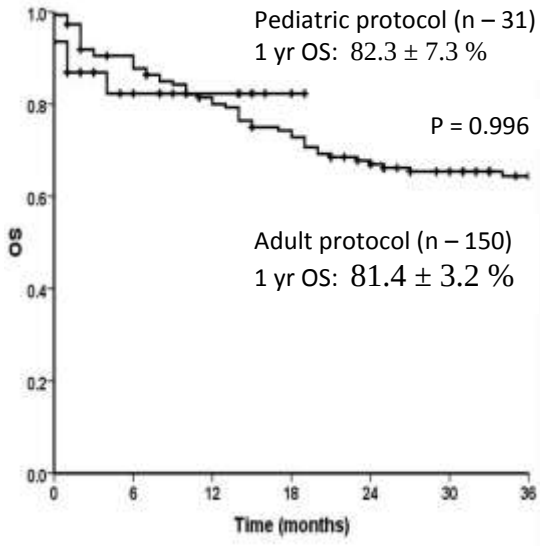


Figure 6b: Event free survival

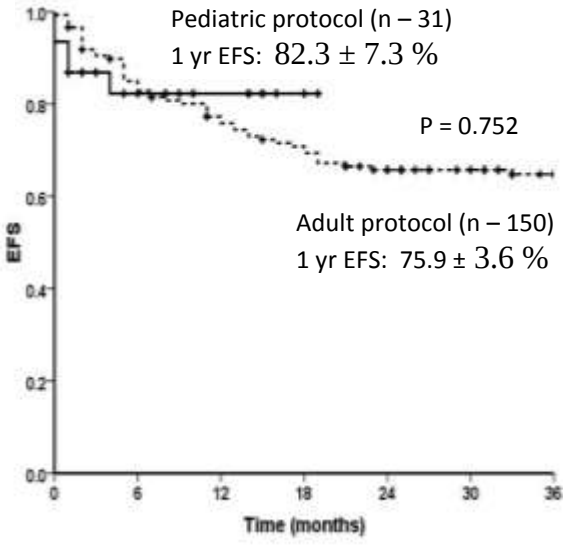


Figure 6a: Kaplan Meier curves for overall survival (OS) in adolescents **(≥ 15 ≤ 20 yrs)** treated with intermediate risk pediatric protocol (n = 31) and the modified adult GMALL protocol ((n = 150).
With an actuarial median follow up period of 8(1 - 47) months and 27 (1-118) months those treated with intermediate risk pediatric protocol and the modified adult GMALL protocol;; the one year overall survival was 82.3 ± 7.3 % and 81.4 ± 3.2 % respectively.
(*P* value = 0.996)

Figure 6b: Kaplan Meier curves for event free survival (EFS) in adolescents **(≥ 15 ≤ 20 yrs)** treated with intermediate risk pediatric protocol (n = 31) and the modified adult GMALL protocol ((n = 150).
With an actuarial median follow up period of 7.7(1 - 19) months and 18(1-118) months those treated with intermediate risk pediatric protocol and the modified adult GMALL protocol;the one year event free survival was 82.3 ± 7.3 % and 75.9 ± 3.6 % respectively. (*P* value = 0.752)

Objective 4:

Evaluation of the role of MRD by flow cytometry at end induction

Tube 1 20/10/45/19	Tube 2 22/34/45/19	Tube 3 11a/10/45/19	Tube 4* 38/10/34/19	Tube 5* 58/10/34/19	Tube 6* 123/10/34/19
71.4	57.1	52.4	66.7	33.3	75[a]

Minimal residual disease (MRD) Definition:(88)

Definition	Values in %
MRD Positive	≥ 0.01
MRD Negative	< 0.01

Table 20: Leukemia associated immunophenotype (LAIP) statistics	
Newly diagnosed patients in whom LAIP attempted at diagnosis by flow cytometry	**n (%) n = 106**
(i) NO LAIP	3(2.8)
(ii) LAIP identified at diagnosis	**103(97)**
(a) LAIP available and evaluated at end induction	**75(72)**
• MRD positive (≥ 0.01 %)	22(29.3)
• MRD negative (< 0.01 %)	53(70.6)
(b) LAIP available at diagnosis but no sample received at end induction	**28(27)**
• Ongoing induction	3(10.7%)
• Induction deaths	6(21.4%)
• Samples not received	9(32.1%)
• Discharged against medical advice	10(35.7%)

Table 21: Baseline characteristics

Variables	MRD (-) n (%) / Median (range) n = 53	MRD (+) n (%) / Median (range) n = 22	P value
Age (years)	6 (1 – 60)	12 (2 -49)	0.071
Sex (male)	33 (62.3)	18	0.285
Physical findings :			
• Hepatomegaly (cm)	3 (1- 8)	3 (1-8)	0.784
• Splenomegaly (cm)	3 (1 – 14)	3 (1 -10)	0.844
• CNS Disease (%)	9 (17.0)	4	1.000
• Pleural Effusion (%)	**0**	0	-
• Mediastinal mass (%)	**0**	0	-
• Testicular mass (%)	**1 (2.6)**	1 (5.9)	0.527
Lab Parameters : WBC (10^9 / Lt)	7.7 (0.7 – 174.5)	17.4 (0.7 -154.6)	0.118

No significant difference in the baseline demographics in the two groups

Table 22: Cytogenetics, molecular genetics and risk status			
Variables	**MRD (-) n (%) / Median (range) n- 53**	**MRD (+) n (%) / Median (range) n – 22**	**P value**
Cytogenetics :			
▪ Poor	6 (11.3)	8 (36.3)	
RT PCR :	51 (96.2)	21 (95.5)	1.000
▪ BCR ABL	2 (3.9)	5 (22.7)	0.020
▪ TEL AML	8 (16.3)	1 (4.5)	0.101
▪ MLL	0(0%)	0(0%)	-
▪ E2A PBX	3 (6.1)	1 (4.5)	1.000
Overall Risk :			
▪ SR	16 (30.1)	4 (18.1)	**0.001**
▪ IR	32 (60.3)	9 (40.9)	
▪ HR	5 (9.4)	9 (40.9)	

Overall risk stratification showed a significant difference between the MRD (-) and MRD (+) groups.

Table 23 : Protocols , response outcomes

Variables	MRD (-) n (%) / Median (range) n- 53	MRD (+) n (%) / Median (range) n – 22	P value
Protocols :			
IR MD MTx	14 (26.4) (1 later changed to R1R2)	5 (22.7)	0.106
IR RT/No MTx	21 (39.6)	11 (50.0)	
▪ Modified GMALL	6 (11.3)	8 (36.3)	
▪ SR (No MTX/No RT)	5 (9.4)	3 (3.6)	
▪ SR MD Tx	7 (13.2)	-	
Prednisolone Response (PR): n	33 (62.6)	19 (86.3)	0.084
▪ GPR (Good)	32 (96.9)	15 (78.9	
▪ PPR (Poor)	1 (3)	4 (21)	
End Induction Remission status :			*0.214*
▪ CR (Complete remission)	52 (98.1)	20 (90.0)	
▪ RD (Residual disease)	1 (1.8)	2 (9.0)	

Table 24: Follow up of Outcome			
Variables	**MRD (-) n (%) / Median (range) n- 53**	**MRD (+) n (%) / Median (range) n – 22**	**P value**
Maintanence:			0.015
▪ Yes	29 (54.7)	8 (36.3)	
▪ No	24 (45.2)	14 (63.6)	
i. In pre-maintenance phase	21(87.5)	9 (64.2)	
ii. Induction Deaths	-	-	-
iii. Death due to progressive disease	1(4.1)	3 (33.3)	
iv. No Follow up	1(4.1)	1 (33.3)	
v. Changed to R1R2	1(4.1)	-	-
vi. Refractory disease – No follow up	-	2 (22.2)	-
Relapse	1 (1.8)	3 (13.6)	0.073
▪ Very early	1 (1.8)	2 (13.6)	
▪ Alive	52 (98.1)	19 (86.4)	
In Complete remission (CR), on treatment	49	17	0.146
CCR (Continuous complete remission)	0	0	-

Survival statistics: **(Figures 7a - 8b)**

The overall survival (OS) and the event free survival (EFS) were calculated using the Kaplan- Meier estimates.

OS in MRD (-) and MRD (+) cohort: **(Figure 7a, 8a)**

At the time of this analysis, the 1 year overall survival of the MRD (-) cohort (n = 53) was 97.4 ± 2.6 % with an actuarial median follow up of 8.3 (1-19) months and 1 year overall survival of MRD (+) cohort (n = 22) was 83.1 ± 9.0 % with an actuarial median follow up of 7.5 (1-13) months. For the purpose of this analysis, patients who had relapsed during therapy and then subsequently lost to follow up were considered as dead, 30 days after the last follow up.

A log rank comparison among those treated with the MRD (-) cohort and the MRD (+) cohort showed a statistically significant survival difference. (P = 0.035).

EFS in MRD (-) and MRD (+) cohort: **(Figure 7b, 8b)**

At the time of this analysis, the 1 year event free survival of the MRD (-) cohort (n = 53) was 97.4 ± 2.5 % with an actuarial median follow up of 7.7 (1-19) months. The 1 year event free survival for the MRD (+) cohort (n = 22) was 58.2 ± 18.4 % with an actuarial median follow up of 7.4 (1- 13) months. An event was considered whenever there was a relapse or death. In

cases where death was secondary to relapse and progressive disease, the date of relapse was considered an event in that patient.

A log rank comparison among those treated with the MRD (-) and MRD (+) showed a statistically significant survival difference. (*P* = 0.002).

Figure 7a: Overall survival

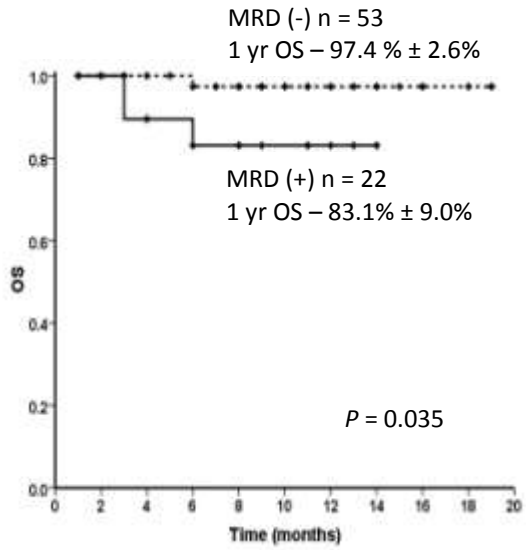


Figure 7b: Event free survival

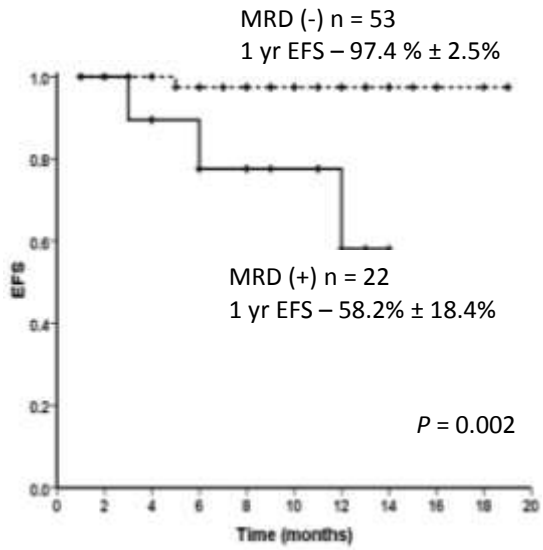


Figure 7a: Kaplan Meier curves for overall survival (OS) in MRD (-) (n = 53) and MRD (+) patients (n = 22)
With an actuarial median follow up of 8.3 (1-19) months and 7.5 (1-13) months; the one year overall survival of the MRD (-) cohort (n = 53) was 97.4 ± 2.6 % and for the MRD (+) cohort (n = 22) was 83.1 ± 9.0 % respectively. (*P* value = 0.035).

Figure 7b: Kaplan Meier curves for event free survival (EFS) in MRD (-) and MRD (+) patients.
With an actuarial median follow up of 7.7 (1-19) months and 7.4 (1- 13) months; the one year event free survival of the MRD (-) cohort (n = 53) was 97.4 ± 2.5 % and for the MRD (+) cohort (n = 22) was 58.2 ± 18.4 % respectively. (*P* value = 0.002).

Figure 8a: Overall survival

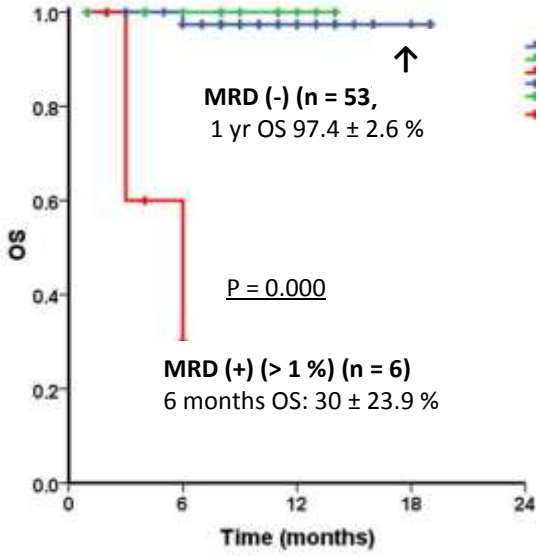


Figure 8b: Event free survival

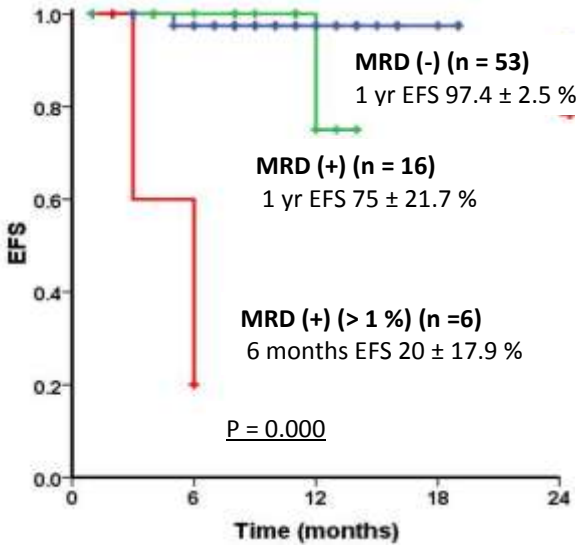


Figure 8a: Comparison of Kaplan Meier curves for overall survival (OS) of MRD (-) (< 0.001%)] and MRD strongly (+) (>1 %)

With an actuarial median follow up of 8.3 (1-19) months, the 6 months and 1 year OS in MRD (-) cohort (n = 53) is 1 yr OS 97.4 ± 2.6 %. With a median follow up of 6 months, the 6 months OS in MRD strongly (+) cohort (n = 6) is 30 ± 23.9 %.
A log rank comparison between the two groups of MRD (-) and MRD strongly (+) showed a significant survival difference. (P = 0.000)

Figure 8b: Comparison of Kaplan Meier curves for event free survival (OS) of MRD (-) (< 0.001%)] , MRD (+) (>0.001%)] and MRD strongly (+) (>1 %)

With an actuarial median follow up of 7.7 (1-19) months, the 6 months and 1 year EFS in MRD (-) cohort (n = 53) is 97.4 ± 2.6 %. With an actuarial median follow up of 7.7 (1-13) months, the 6 months and 1 year EFS in MRD (+) cohort (n = 16) is 75 ± 21.7 %. With a median follow up of 6 months, the 6 months OS in MRD strongly (+) cohort (n = 6) is 20 ± 17.9 %.
A log rank comparison between the two groups of MRD (-) and MRD strongly (+) showed a significant survival difference. (P = 0.000)

Discussion:

Objective 1:

This study reports the baseline demographics, laboratory features including the immunophenotype, cytogenetic and their molecular data and the long-term outcomes of adult ALL following treatment with a modified GMALL protocol.

On comparing the baseline demographics, we found a median age of 26 years; much lower than the reported median age of 33 years in many adult ALL trials. (26) The large number of adolescent patients can explain the reported lower median age in the present study. We also found a male predominance in our study cohort.

Extra medullary manifestations in the form of CNS involvement (14.1 %) was found to be much higher than the available reported literature of around 5 %. (93)

Among the available laboratory data, the median WBC count was 9.5 x 10^{9} /Lt. The incidence of B cell, T cell ALL and Philadelphia positivity in our adult study was also similar to that reported in literature (42) .

Treatment outcome was available in 455 adults. The standard risk as well as high-risk patients was all treated with the same modified adult GMALL protocol. Imatinib was added in all patients with Philadelphia positivity.

End induction complete remission rates in our study group was 83.2 %, which is comparable to most of the adult reported studies.(26) We also found an induction death rate of 6.3 %, predominantly due to neutropenic bacterial sepsis.

27 % of our patients are presently in complete continuous remission (CCR) and additionally 22.6 % of our patient cohort is receiving chemotherapy and is in complete remission. 29 % of our patient cohort relapsed, with most of them having a very early relapse. 39.3 % of our patients died, with majority (78.2 %) of them having died due to progressive disease and 21.8 % deaths due to infection.

Overall, with a median follow up period of 65 months, the five-year event free survival was 50.1 ± 2.9 % and five year overall survival was 51.6 ± 2.9 %. (26) The higher outcomes in our study could also be due to a larger number of young adults treated in our patient cohort. This reported outcome is significant in terms of available literature being reported from a developing country, where in cancer treatment related government funding is much less than the developed countries.

Major costs involved in treatment of adult ALL are attributed to the use of high dose methotrexate as part of consolidation instead of the cranial irradiation. The overall costs involved in the treatment of a single patient is less than 8000 $, amounting to approximately 5, 00,000 Indian currency.

Considering the costs involved due to the socio economic status and the results achieved, this treatment protocol is quite effective and is widely recommended.

Objective 2:

(i) Standard risk acute lymphoblastic leukemia:

A comparison of the two standard risk protocols (SR BFM 95 and SR study protocol) used in our department did not demonstrate any significant difference in their baseline presenting demographics or their baseline molecular or cytogenetic profile at presentation.

On comparing the two groups on the basis of their relapse rates, though there was a lower incidence of relapse in the BFM 95 group, there was no significant statistical difference between the two groups. More follow up is needed to accurately identify the relapse rate in the two groups.

Overall, there was no significant difference in the 3 year OS and the EFS between the two groups. The overall outcomes of the children treated with the BFM 95 regimens was found to be similar to the published literature (57).

A significant difference between the two groups is the total amount of cost involved. A standard risk B cell ALL treated on the BFM 95 regimens requires atleast 7,000 $ while a standard risk B cell ALL treated on non-methotrexate / non-radiation based (study) protocol requires a maximum of 6,000 $.

Though the actuarial median follow up is short, the non methotrexate / non radiation based study protocol can be considered as an effective regimen in economically deprived children, with a little support from the state funding agencies.

(ii) **Intermediate risk acute lymphoblastic leukemia:**

A comparison of the two intermediate risk protocols (IR BFM 95 and Radiation based protocol) used in our department did not demonstrate any significant difference in their baseline presenting features.

The significant difference in the cytogenetic and the molecular profile between the two groups could be attributed to few high risk children who were continued to be treated on the radiation based treatment regimen due to financial limitations, thereby unable to afford high risk protocol and a transplant.

On comparing the two groups on the basis of their relapse rates, the radiation-based protocol had a much higher incidence of relapse in comparison to the BFM 95 based protocol, though the follow up was much shorter in the latter.

Overall, there was no significant difference in the 2 year OS and the EFS between the two groups. The overall outcomes of the children treated with the BFM 95 regimens was found to be similar to the published literature (57).

A significant difference between the two groups is the total amount of cost involved. An intermediate risk ALL treated on the BFM 95 regimens requires atleast 7,500 $ while radiation (non-methotrexate) based protocol requires a maximum of 6,500 $.

Though the actuarial median follow up is short in the BFM 95 based protocol, based on the 2 year outcomes, we can conclude that the radiation based study protocol can be considered as an effective regimen in economically deprived children, with a little support from the state funding agencies.

Objective 3:

A comparison of the two adolescent age groups treated with pediatric intermediate risk protocol and the adult GMALL protocol, in our department did not demonstrate any significant difference in their baseline presenting demographics or their baseline molecular or cytogenetic profile at presentation.

A significant difference was the use of cranial irradiation for every adolescent in the adult GMALL group, whereas in adolescents with B cell leukemia on pediatric intermediate risk group protocol receiving the methotrexate based therapy did not receive cranial irradiation unless they have CNS III disease. All adolescents with the T cell leukemia on pediatric intermediate risk group protocol received at least prophylactic

A higher number of relapses were seen in the adolescent age group receiving the adult GMALL group but this can be explained by the extremely short follow up available in group receiving pediatric intermediate risk group protocol. There were no major toxicities noted in the adolescent group receiving pediatric regimens.

The three year OS and EFS in adolescents treated with adult GMALL protocol were 64.8 ± 4.0 % and 64.4 ± 4.1 % respectively.

Though, follow up data of the overall survival and event free survival of the two groups at the end of one year does not show any statistically significant difference, the superiority of pediatric protocols over the adult protocols as demonstrated in various international trials remains to be established in the Indian cohort. A much longer follow up would be required for the same, though there appears to be a trend towards improvement.

The issue of cost difference between the two protocols also needs a special mention. Those treated with the adult GMALL regimens would require atleast 8000 $ for their complete therapy as compared to a total of 6500 to 7500 $ for those treated with the intermediate risk pediatric based protocol.

Objective 4:

Usefulness of minimal residual disease as a prognostic marker has already been explored. Using flow cytometry to identify LAIP (leukemia associated immunophenotype) has helped in further stratifying B cell acute lymphoblastic leukemia (ALL). Though multiple end points have been shown to have their individual significance, we had chosen end induction bone marrow sample for flow cytometry using 6 recently standardized tubes containing specific antibodies against specific leukemia associated antigens.

Using the mentioned combination of antibodies, LAIP could be identified in 97 % of the total B cell leukemia, which is comparable to the published studies. (88)

As shown in the results, there was only one standard risk ALL in the MRD (-) cohort who relapsed. Though the follow up is short, still a majority (92.4 %) of the total MRD (-) cohort were in complete remission (CR) inspite of this cohort having significant number (9.4 %) of high-risk cases.

Among the MRD (+) cohort, 2 patients who had a residual disease at the end of induction were found to be strongly MRD positive (> 1 %). Both patients opted for palliative therapy. Among the entire MRD (+) cohort, there were 3 relapses in comparison to the MRD (-)

cohort. Out of these 3 patients, one was a standard risk adult ALL, one intermediate risk pediatric ALL and the third was a high risk Philadelphia positive ALL. Though the numbers are small, it is in the standard and the intermediate risk ALL, the usefulness of MRD by flowcytometry is demonstrated and an early intensification of the therapy or a bone marrow transplant might yield better results in the near future.

Since the follow up was short, none of the patients in both the cohort have completed their therapy.

Conclusions:

I. Using the current modified GMALL regimens in adults (≥ 15 years); treatment outcomes were comparable to those reported in the international literature. This has special implications in resource limited countries where government sponsored funding is limited and majority of the cost of therapy has to be borne by the patient and his family.

II. Using BFM 95 regimens in standard risk and intermediate risk children (≥ 1 < 15 years) with acute lymphoblastic leukemia, short term outcomes were similar to that reported in the international literature. There was no major difference noted in the two standard risk and two intermediate risk protocols. Long term follow up would be required to accurately establish its effectiveness in the Indian cohort.

III. Using pediatric regimens in adolescent age group (≥15 ≤ 20 years) did not reveal any significant difference in the overall outcome as compared to the adult regimens. Though the follow up is short, pediatric regimens are feasible in adolescents with minimal toxicity. It remains to be seen whether using pediatric regimens will improve long term survivals in the Indian cohort, though there appears to be a trend towards improvement in their outcomes with pediatric regimens.

IV. Using flow cytometry in detecting minimal residual disease can significantly identify high risk patients and improve their outcome by timely intensification.

Bibliography:

1. Pui C-H, Evans WE. Treatment of Acute Lymphoblastic Leukemia. N Engl J Med. 2006;354(2):166–78.

2. Stanulla M, Schrappe M. Treatment of Childhood Acute Lymphoblastic Leukemia. Semin Hematol. 2009 Jan;46(1):52–63.

3. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics, 2006. CA Cancer J Clin. 2006 Apr;56(2):106–30.

4. Gökbuget N, Hoelzer D. Treatment of Adult Acute Lymphoblastic Leukemia. Semin Hematol. 2009 Jan;46(1):64–75.

5. Moricke A, Zimmermann M, Reiter A, Henze G, Schrauder A, Gadner H, et al. Long-term results of five consecutive trials in childhood acute lymphoblastic leukemia performed by the ALL-BFM study group from 1981 to 2000. Leukemia. 2009 Dec 10;24(2):265–84.

6. Silverman LB, Gelber RD, Dalton VK, Asselin BL, Barr RD, Clavell LA, et al. Improved outcome for children with acute lymphoblastic leukemia: results of Dana-Farber Consortium Protocol 91-01. Blood. 2001 Mar 1;97(5):1211–8.

7. Kaspers GJ., Veerman AJ., Pieters R, Van Zantwijk CH, Smets LA, Van Wering ER, et al. In Vitro Cellular Drug Resistance and Prognosis in Newly Diagnosed Childhood Acute Lymphoblastic Leukemia. Blood. 1997 Oct 1;90(7):2723–9.

8. Pulte D, Gondos A, Brenner H. Improvement in survival in younger patients with acute lymphoblastic leukemia from the 1980s to the early 21st century. Blood. 2009 Feb 12;113(7):1408 –1411.

9. Bajel A, George B, Mathews V, Viswabandya A, Kavitha ML, Srivastava A, et al. Adult ALL: treatment outcome and prognostic factors in an Indian population using a modified German ALL (GMALL) protocol. Leukemia. 2007 Jun 7;21(10):2230–3.

10. Redaelli A, Laskin BL, Stephens JM, Botteman MF, Pashos CL. A systematic literature review of the clinical and epidemiological burden of acute lymphoblastic leukaemia (ALL). Eur J Cancer Care (Engl). 2005 Mar;14(1):53–62.

11. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. Int J Cancer J Int Cancer. 2008 Jun 1;122(11):2607–11.

12. Linabery AM, Ross JA. Trends in childhood cancer incidence in the U.S. (1992-2004). Cancer. 2008 Jan 15;112(2):416–32.

13. Chandy M. Childhood acute lymphoblastic leukemia in India: an approach to management in a three-tier society. Med Pediatr Oncol. 1995 Sep;25(3):197–203.

14. Pui C-H, Sandlund JT, Pei D, Rivera GK, Howard SC, Ribeiro RC, et al. Results of therapy for acute lymphoblastic leukemia in black and white children. JAMA J Am Med Assoc. 2003 Oct 15;290(15):2001–7.

15. Magrath I, Shanta V, Advani S, Adde M, Arya LS, Banavali S, et al. Treatment of acute lymphoblastic leukaemia in countries with limited resources; lessons from use of a single protocol in India over a twenty year period [corrected]. Eur J Cancer Oxf Engl 1990. 2005 Jul;41(11):1570–83.

16. Bajel A, George B, Mathews V, Viswabandya A, Kavitha ML, Srivastava A, et al. Treatment of children with acute lymphoblastic leukemia in India using a BFM protocol. Pediatr Blood Cancer. 2008 Nov;51(5):621–5.

17. Howard SC, Metzger ML, Wilimas JA, Quintana Y, Pui C-H, Robison LL, et al. Childhood cancer epidemiology in low-income countries. Cancer. 2008 Feb 1;112(3):461–72.

18. Mostert S, Sitaresmi MN, Gundy CM, Sutaryo, Veerman AJP. Influence of socioeconomic status on childhood acute lymphoblastic leukemia treatment in Indonesia. Pediatrics. 2006 Dec;118(6):e1600–1606.

19. Rajajee S, Desikulu MV, Pushpa V. Survival of childhood acute lymphoblastic leukemia: experience in Chennai. J Trop Pediatr. 1999 Dec;45(6):367–70.

20. Bennett JM, Catovsky D, Daniel M, Flandrin G, Galton DAG, Gralnick HR, et al. Proposals for the Classification of the Acute Leukaemias French-American-British (FAB) Co-operative Group. Br J Haematol. 1976 Aug 1;33(4):451–8.

21. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, et al. The morphological classification of acute lymphoblastic leukaemia: concordance among observers and clinical correlations. Br J Haematol. 1981 Apr;47(4):553–61.

22. Davey FR, Castella A, Lauenstein K, Hubbell C, Oates RP. Prognostic significance of the revised French-American-British classification for acute lymphocytic leukaemia. Clin Lab Haematol. 1983;5(4):343–51.

23. Bene MC, Castoldi G, Knapp W, Ludwig WD, Matutes E, Orfao A, et al. Proposals for the immunological classification of acute leukemias. European Group for the Immunological Characterization of Leukemias (EGIL). Leuk Off J Leuk Soc Am Leuk Res Fund UK. 1995 Oct;9(10):1783–6.

24. Pui CH, Behm FG, Crist WM. Clinical and biologic relevance of immunologic marker studies in childhood acute lymphoblastic leukemia. Blood. 1993 Jul 15;82(2):343–62.

25. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid

neoplasms and acute leukemia: rationale and important changes. Blood. 2009 Jul 30;114(5):937–51.

26. Gökbuget N, Hoelzer D. Treatment of Adult Acute Lymphoblastic Leukemia. Semin Hematol. 2009 Jan;46(1):64–75.

27. Induction therapy by frequent administration of doxorubicin with four other drugs, followed by intensive consolidation and maintenance therapy for adult acute lymphoblastic leukemia: the JALSG-ALL93 study.

28. Rowe JM, Buck G, Burnett AK, Chopra R, Wiernik PH, Richards SM, et al. Induction Therapy for Adults with Acute Lymphoblastic Leukemia: Results of More Than 1500 Patients from the International ALL Trial: MRC UKALL XII/ECOG E2993. Blood. 2005 Dec 1;106(12):3760–7.

29. Larson RA, Dodge RK, Linker CA, Stone RM, Powell BL, Lee EJ, et al. A Randomized Controlled Trial of Filgrastim During Remission Induction and Consolidation Chemotherapy for Adults With Acute Lymphoblastic Leukemia: CALGB Study 9111. Blood. 1998 Sep 1;92(5):1556–64.

30. Kantarjian HM, Jeha S, Gandhi V, Wess M, Faderl S. Clofarabine: past, present, and future. Leuk Lymphoma. 2007 Oct;48(10):1922–30.

31. Annino L, Vegna ML, Camera A, Specchia G, Visani G, Fioritoni G, et al. Treatment of Adult Acute Lymphoblastic Leukemia (ALL): Long-Term Follow-up of the GIMEMA ALL 0288 Randomized Study. Blood. 2002 Feb 1;99(3):863–71.

32. Hoelzer D, Thiel E, Löffler H, Büchner T, Ganser A, Heil G, et al. Prognostic factors in a multicenter study for treatment of acute lymphoblastic leukemia in adults. Blood. 1988 Jan;71(1):123–31.

33. Gökbuget N, Hoelzer D. Treatment of Adult Acute Lymphoblastic Leukemia. ASH Educ Program Book. 2006 Jan 1;2006(1):133–41.

34. Go□kbuget N. Intensification of induction and consolidation improves only subgroups of adult ALL: analysis of 1200 patients in GMALL study. Blood. 2001;(98):802a.

35. Maung ZT, Reid MM, Matheson E, Taylor PR, Proctor SJ, Hall AG. Corticosteroid resistance is increased in lymphoblasts from adults compared with children: preliminary results of in vitro drug sensitivity study in adults with acute lymphoblastic leukaemia. Br J Haematol. 1995 Sep;91(1):93–100.

36. Styczynski J, Pieters R, Huismans DR, Schuurhuis GJ, Wysocki M, Veerman AJ. In vitro drug resistance profiles of adult versus childhood acute lymphoblastic leukaemia. Br J Haematol. 2000 Sep;110(4):813–8.

37. Jeha S. Who should be treating adolescents and young adults with acute lymphoblastic leukaemia? Eur J Cancer Oxf Engl 1990. 2003 Dec;39(18):2579–83.

38. Pulte D, Gondos A, Brenner H. Trends in 5- and 10-Year Survival After Diagnosis with Childhood Hematologic Malignancies in the United States, 1990–2004. J Natl Cancer Inst. 2008 Sep 17;100(18):1301–9.

39. Dini G, Banov L, Dini S. Where should adolescents with ALL be treated? Bone Marrow Transpl. 42(S2):S35–S39.

40. Chessells JM, Hall E, Prentice HG, Durrant J, Bailey CC, Richards SM. The impact of age on outcome in lymphoblastic leukaemia; MRC UKALL X and XA compared: a report from the MRC Paediatric and Adult Working Parties. Leuk Off J Leuk Soc Am Leuk Res Fund UK. 1998 Apr;12(4):463–73.

41. Borkhardt A, Cazzaniga G, Viehmann S, Valsecchi MG, Ludwig WD, Burci L, et al. Incidence and Clinical Relevance of TEL/AML1 Fusion Genes in Children With Acute Lymphoblastic Leukemia Enrolled in the German and Italian Multicenter Therapy Trials. Blood. 1997 Jul 15;90(2):571–7.

42. DeAngelo DJ. The Treatment of Adolescents and Young Adults with Acute Lymphoblastic Leukemia. ASH Educ Program Book. 2005 Jan 1;2005(1):123–30.

43. Schafer ES, Hunger SP. Optimal therapy for acute lymphoblastic leukemia in adolescents and young adults. Nat Rev Clin Oncol. 2011 May 31;8(7):417–24.

44. Stock W, La M, Sanford B, Bloomfield CD, Vardiman JW, Gaynon P, et al. What Determines the Outcomes for Adolescents and Young Adults with Acute Lymphoblastic Leukemia Treated on Cooperative Group Protocols? A Comparison of Children's Cancer Group and Cancer and Leukemia Group B Studies. Blood. 2008 Sep 1;112(5):1646–54.

45. Boissel N, Auclerc M-F, Lhéritier V, Perel Y, Thomas X, Leblanc T, et al. Should Adolescents With Acute Lymphoblastic Leukemia Be Treated as Old Children or Young Adults? Comparison of the French FRALLE-93 and LALA-94 Trials. J Clin Oncol. 2003 Mar 1;21(5):774–80.

46. Bont JM de, Holt B van der, Dekker AW, Berg A van der D den, Sonneveld P, Pieters R. Significant difference in outcome for adolescents with acute lymphoblastic leukemia treated on pediatric vs adult protocols in the Netherlands. Leukemia. 2004 Oct 14;18(12):2032–5.

47. Testi AM. Difference in outcome of adolescents with acute lymphoblastic leukemia (ALL) enrolled in pediatric (AIEOP) and adult (GIMEMA) protocols. Blood. 2004;(104):1954.

48. Ramanujachar R, Richards S, Hann I, Goldstone A, Mitchell C, Vora A, et al. Adolescents with acute lymphoblastic leukaemia: outcome on UK national paediatric (ALL97) and adult (UKALLXII/E2993) trials. Pediatr Blood Cancer. 2007 Mar;48(3):254–61.

49. López-Hernández MA, Alvarado-Ibarra M, Jiménez-Alvarado RM, De Diego-Flores JE, González-Avante CM. [Adolescents with de novo acute lymphoblastic leukemia: efficacy and safety of a pediatric vs adult treatment protocol]. Gac Médica México. 2008 Dec;144(6):485–9.

50. Usvasalo A, Räty R, Knuutila S, Vettenranta K, Harila-Saari A, Jantunen E, et al. Acute Lymphoblastic Leukemia in Adolescents and Young Adults in Finland. Haematologica. 2008 Aug 1;93(8):1161–8.

51. Ribera J-M, Oriol A. Acute lymphoblastic leukemia in adolescents and young adults. Hematol Oncol Clin North Am. 2009 Oct;23(5):1033–1042, vi.

52. Mastrangelo R, Poplack D, Bleyer A, Riccardi R, Sather H, D'Angio G. Report and recommendations of the rome workshop concerning poor-prognosis acute lymphoblastic leukemia in children: Biologic bases for staging, stratification, and treatment. Med Pediatr Oncol. 1986 Jan 1;14(3):191–4.

53. Smith M, Arthur D, Camitta B, Carroll AJ, Crist W, Gaynon P, et al. Uniform approach to risk classification and treatment assignment for children with acute lymphoblastic leukemia. J Clin Oncol. 1996 Jan 1;14(1):18–24.

54. Vrooman LM, Silverman LB. Childhood acute lymphoblastic leukemia: update on prognostic factors. Curr Opin Pediatr. 2009 Feb;21(1):1–8.

55. Moghrabi A, Levy DE, Asselin B, Barr R, Clavell L, Hurwitz C, et al. Results of the Dana-Farber Cancer Institute ALL Consortium Protocol 95-01 for Children with Acute Lymphoblastic Leukemia. Blood. 2007 Feb 1;109(3):896–904.

56. Bürger B, Zimmermann M, Mann G, Kühl J, Löning L, Riehm H, et al. Diagnostic Cerebrospinal Fluid Examination in Children With Acute Lymphoblastic Leukemia: Significance of Low Leukocyte Counts With Blasts or Traumatic Lumbar Puncture. J Clin Oncol. 2003 Jan 15;21(2):184–8.

57. Möricke A, Reiter A, Zimmermann M, Gadner H, Stanulla M, Dördelmann M, et al. Risk-Adjusted Therapy of Acute Lymphoblastic Leukemia Can Decrease Treatment Burden and Improve Survival: Treatment Results of 2169 Unselected Pediatric and Adolescent Patients Enrolled in the Trial ALL-BFM 95. Blood. 2008 May 1;111(9):4477–89.

58. Pieters R, Schrappe M, De Lorenzo P, Hann I, De Rossi G, Felice M, et al. A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-

99): an observational study and a multicentre randomised trial. The Lancet. 21;370(9583):240–50.

59. Nachman JB, Heerema NA, Sather H, Camitta B, Forestier E, Harrison CJ, et al. Outcome of Treatment in Children with Hypodiploid Acute Lymphoblastic Leukemia. Blood. 2007 Aug 15;110(4):1112–5.

60. Moorman AV, Richards SM, Robinson HM, Strefford JC, Gibson BES, Kinsey SE, et al. Prognosis of Children with Acute Lymphoblastic Leukemia (ALL) and Intrachromosomal Amplification of Chromosome 21 (iAMP21). Blood. 2007 Mar 15;109(6):2327–30.

61. Aricò M, Valsecchi MG, Camitta B, Schrappe M, Chessells J, Baruchel A, et al. Outcome of Treatment in Children with Philadelphia Chromosome–Positive Acute Lymphoblastic Leukemia. N Engl J Med. 2000;342(14):998–1006.

62. Borowitz MJ, Devidas M, Hunger SP, Bowman WP, Carroll AJ, Carroll WL, et al. Clinical significance of minimal residual disease in childhood acute lymphoblastic leukemia and its relationship to other prognostic factors: a Children's Oncology Group study. Blood. 2008 Jun 15;111(12):5477–85.

63. Sutcliffe MJ, Shuster JJ, Sather HN, Camitta BM, Pullen J, Schultz KR, et al. High concordance from independent studies by the Children's Cancer Group (CCG) and Pediatric Oncology Group (POG) associating favorable prognosis with combined

trisomies 4, 10, and 17 in children with NCI Standard-Risk B-precursor Acute Lymphoblastic Leukemia: a Children's Oncology Group (COG) initiative. Leukemia [Internet]. 2005 Mar 24 [cited 2012 Mar 11];19(5). Available from: http://www.nature.com/leu/journal/v19/n5/full/2403673a.html

64. Schultz KR, Pullen DJ, Sather HN, Shuster JJ, Devidas M, Borowitz MJ, et al. Risk- and Response-Based Classification of Childhood B-Precursor Acute Lymphoblastic Leukemia: A Combined Analysis of Prognostic Markers from the Pediatric Oncology Group (POG) and Children's Cancer Group (CCG). Blood. 2007 Feb 1;109(3):926–35.

65. Rubnitz JE, Wichlan D, Devidas M, Shuster J, Linda SB, Kurtzberg J, et al. Prospective Analysis of TEL Gene Rearrangements in Childhood Acute Lymphoblastic Leukemia: A Children's Oncology Group Study. J Clin Oncol. 2008 May 1;26(13):2186–91.

66. Gajjar A, Ribeiro R, Hancock M, Rivera G, Mahmoud H, Sandlund J, et al. Persistence of circulating blasts after 1 week of multiagent chemotherapy confers a poor prognosis in childhood acute lymphoblastic leukemia. Blood. 1995;86(4):1292 –1295.

67. Schrappe M, Reiter A, Zimmermann M, Harbott J, Ludwig WD, Henze G, et al. Long-term results of four consecutive trials in childhood ALL performed by the ALL-BFM study group from 1981 to 1995. Berlin-Frankfurt-Münster. Leuk Off J Leuk Soc Am Leuk Res Fund UK. 2000 Dec;14(12):2205–22.

68. Stock W. Adolescents and Young Adults with Acute Lymphoblastic Leukemia. ASH Educ Program Book. 2010 Dec 4;2010(1):21–9.

69. Smith MA, Seibel NL, Altekruse SF, Ries LAG, Melbert DL, O'Leary M, et al. Outcomes for Children and Adolescents With Cancer: Challenges for the Twenty-First Century. J Clin Oncol. 2010 May 20;28(15):2625–34.

70. Silverman LB, Supko JG, Stevenson KE, Woodward C, Vrooman LM, Neuberg DS, et al. Intravenous PEG-Asparaginase During Remission Induction in Children and Adolescents with Newly Diagnosed Acute Lymphoblastic Leukemia. Blood. 2010 Feb 18;115(7):1351–3.

71. Schrappe M, Reiter A, Riehm H. Cytoreduction and prognosis in childhood acute lymphoblastic leukemia. J Clin Oncol Off J Am Soc Clin Oncol. 1996 Aug;14(8):2403–6.

72. Ryan DH. Detection of residual disease in acute leukemia using immunological markers, in Bennett JM, Foon KA (eds): Immunologic Approaches to the Classification and Management of Lymphomas and Leukemias. Norwell,MA: Kluwer Academic; 1988. pg 173 p.

73. Campana D, Pui CH. Detection of minimal residual disease in acute leukemia: methodologic advances and clinical significance [see comments]. Blood. 1995;85(6):1416–34.

74. Van Bekkum DW. Residual reflections on the detections and treatment of leukemia in B Lowenberg, Hagenbeek A (eds) : Minimal residual disease in acute leukemias . Boston, MA: Martinus Nijhoff, 1984, p 385; 1984. page 385 p.

75. Dario Campana. Role of minimal residual disease monitoring in adult and pediatric acute lymphoblastic leukemia. Hematol Oncol Clin North Am. 2009 Oct;23(5):1083–98.

76. Campana D. Minimal Residual Disease in Acute Lymphoblastic Leukemia. ASH Educ Program Book. 2010 Dec 4;2010(1):7–12.

77. Van Dongen JJ, Seriu T, Panzer-Grümayer ER, Biondi A, Pongers-Willemse MJ, Corral L, et al. Prognostic value of minimal residual disease in acute lymphoblastic leukaemia in childhood. Lancet. 1998 Nov 28;352(9142):1731–8.

78. Brisco MJ, Condon J, Hughes E, Neoh SH, Sykes PJ, Seshadri R, et al. Outcome prediction in childhood acute lymphoblastic leukaemia by molecular quantification of residual disease at the end of induction. Lancet. 1994 Jan 22;343(8891):196–200.

79. Coustan-Smith E, Sancho J, Hancock ML, Boyett JM, Behm FG, Raimondi SC, et al. Clinical importance of minimal residual disease in childhood acute lymphoblastic leukemia. Blood. 2000 Oct 15;96(8):2691 –2696.

80. Campana D, Coustan-Smith E. Detection of minimal residual disease in acute leukemia by flow cytometry. Cytometry. 1999 Aug 15;38(4):139–52.

81. Coustan-Smith E, Sancho J, Behm FG, Hancock ML, Razzouk BI, Ribeiro RC, et al. Prognostic Importance of Measuring Early Clearance of Leukemic Cells by Flow Cytometry in Childhood Acute Lymphoblastic Leukemia. Blood. 2002 Jul 1;100(1):52–8.

82. Pui C-H, Campana D, Pei D, Bowman WP, Sandlund JT, Kaste SC, et al. Treatment of Childhood Acute Lymphoblastic Leukemia Without Prophylactic Cranial Irradiation. N Engl J Med. 2009 Jun 25;360(26):2730–41.

83. Bruggemann M, Schrauder A, Raff T, Pfeifer H, Dworzak M, Ottmann OG, et al. Standardized MRD quantification in European ALL trials: Proceedings of the Second International Symposium on MRD assessment in Kiel, Germany, 18|[ndash]|20 September 2008. Leukemia. 2009 Dec 24;24(3):521–35.

84. Fronkova E, Mejstrikova E, Avigad S, Chik KW, Castillo L, Manor S, et al. Minimal residual disease (MRD) analysis in the non-MRD-based ALL IC-BFM 2002 protocol for childhood ALL: is it possible to avoid MRD testing? Leukemia. 2008 Feb 28;22(5):989–97.

85. Coustan-Smith E, Behm FG, Sanchez J, Boyett JM, Hancock ML, Raimondi SC, et al. Immunological detection of minimal residual disease in children with acute lymphoblastic leukaemia. Lancet. 1998 Feb 21;351(9102):550–4.

86. Basso G, Veltroni M, Valsecchi MG, Dworzak MN, Ratei R, Silvestri D, et al. Risk of Relapse of Childhood Acute Lymphoblastic Leukemia Is Predicted By Flow Cytometric Measurement of Residual Disease on Day 15 Bone Marrow. J Clin Oncol. 2009 Nov 1;27(31):5168–74.

87. Cavé H, van der Werff ten Bosch J, Suciu S, Guidal C, Waterkeyn C, Otten J, et al. Clinical significance of minimal residual disease in childhood acute lymphoblastic leukemia. European Organization for Research and Treatment of Cancer--Childhood Leukemia Cooperative Group. N Engl J Med. 1998 Aug 27;339(9):591–8.

88. Patkar N, Alex AA, B. B, Ahmed R, Abraham A, George B, et al. Standardizing minimal residual disease by flow cytometry for precursor B lineage acute lymphoblastic leukemia in a developing country. Cytometry B Clin Cytom. 2012 Jul 1;82B(4):252–8.

89. Tallen G, Ratei R, Mann G, Kaspers G, Niggli F, Karachunsky A, et al. Long-Term Outcome in Children With Relapsed Acute Lymphoblastic Leukemia After Time-Point and Site-of-Relapse Stratification and Intensified Short-Course Multidrug Chemotherapy: Results of Trial ALL-REZ BFM 90. J Clin Oncol. 2010 May 10;28(14):2339–47.

90. Irving J, Jesson J, Virgo P, Case M, Minto L, Eyre L, et al. Establishment and validation of a standard protocol for the detection of minimal residual disease in B lineage

childhood acute lymphoblastic leukemia by flow cytometry in a multi-center setting; Haematologica. 2009 Jun;94(6):870–4.

91. Moorman AV, Chilton L, Wilkinson J, Ensor HM, Bown N, Proctor SJ. A population-based cytogenetic study of adults with acute lymphoblastic leukemia. Blood. 2010 Jan 14;115(2):206–14.

92. Ensor HM, Schwab C, Russell LJ, Richards SM, Morrison H, Masic D, et al. Demographic, clinical, and outcome features of children with acute lymphoblastic leukemia and CRLF2 deregulation: results from the MRC ALL97 clinical trial. Blood. 2011 Feb 17;117(7):2129–36.

93. Lazarus HM, Richards SM, Chopra R, Litzow MR, Burnett AK, Wiernik PH, et al. Central nervous system involvement in adult acute lymphoblastic leukemia at diagnosis: results from the international ALL trial MRC UKALL XII/ECOG E2993. Blood. 2006 Jul 15;108(2):465–72.

ANNEXURES

Appendix 1: Adult ALL ≥ 15 years
Modified BFM (GMALL) protocol

- **Post induction marrow in remission**
- **No translocation t (9; 22) or t(4;11)**
- **Good Prednisolone Response in B lineage with counts < 30,000/cmm,**
- **T lineage <1,00,000/cmm**

PRE-INDUCTION (1 week)

1. Dexamethasone 5 mg/m^2 iv daily Days 1 & 2
2. Prednisolone 60 mg/m^2 p/o daily Day 3 to Day 7

INDUCTION (Phase I: 2 - 5 wks)

1. Daunorubicin 30 mg/m^2 iv weekly x 4
2. Vincristine 1.4 mg/m^2 (max 2 mg) iv weekly x 4
3. L'Asparaginase 70,000 U/ m^2 (total dose) iv/im/sc in divided doses of 10,000 U daily
4. Prednisolone 60 mg/ m^2 daily x 3 weeks and then taper over 10 days

1 week after completion of Phase I, BM to assess remission status

Phase II: 6 - 9 wks

1. Cyclophosphamide 650 mg/m^2 iv Days 1, 15 and 29
2. AraC 75 mg/m^2 iv x 4 days followed by 3 days rest
   Repeat: 4 cycles

CNS PROPHYLAXIS (Given Concurrently with Phase II Induction)

1. Intrathecal Methotrexate 10 mg/m^2 (max 12.5mg) weekly x 4
2. 2400 Rads Cranial RT prophylaxis

Three weeks rest after Phase II

CONSOLIDATION (13 - 17 wks)

1. Intrathecal Methotrexate 10 mg/m^2 (max 12.5mg) x 1
2. AraC 75 mg/m^2 iv daily x 5 days
3. VP-16 50 mg/M^2 iv daily x 5 days

3 weeks rest

1. Intrathecal Methotrexate 10 mg/m^2 (max 12.5 mg) x 1
2. AraC 75 mg/m^2 iv daily x 5 days
3. VP-16 50 mg/m^2 iv daily x 5 days

3 weeks rest

REINDUCTION (Phase I : 20 - 24 wks

1. Vincristine 1.4 mg/m^2 (max 2 mg) iv weekly x 4
2. Adriamycin 25 mg/m^2 iv weekly x 4
3. Dexamethasone 10 mg/m^2 (max 10 mg) p/o daily x 4 wks and then taper Over 10 days

Phase II: 25 - 26 wks

1. Cyclophosphamide 650 mg/m^2 iv x 1
2. AraC 75 mg/m^2 iv daily x 4 days followed by 3 days rest
   Repeat: 2 cycles

Two weeks rest

MAINTENANCE (29 - 136 wks)

1. 6-Mercaptopurine 60 mg/m^2 p/o daily x 2 years
2. Methotrexate 20 mg/m^2 p/o once a week x 2 years
3. Vincristine 1.4 mg/m^2 (max 2 mg) iv Day 1
4. Dexamethasone 6 mg/m^2 Days 1 - 5
   Repeat vincristine/dexamethasone every month x 2 years
5. Intrathecal Methotrexate 10 mg/m^2 (max 12.5mg) every 3 months

Appendix 2a
Intermediate risk BFM 95

Pediatric ALL : PROTOCOL IV

Intermediate Risk

NO RADIOTHERAPY, HDMTX PROTOCOL (ALL BFM 1995)

- **Age - 6 yr - 15 yrs**
- **WBC > 20,000/cmm**
- **Prednisolone good response**
- **Precursor B, CALLA immunophenotype, T-cell immunophenotype**
- **No translocation t(9;22) or t(4;11)**
- **t (1;19) translocation present**
- **Pro B cell without 11q23.**
- **CNS disease or suspicious CNS disease.**
- **Higher Socio-economic status**

PREINDUCTION **(1 week)**

1. Dexamethasone 6 mg/ m^2 iv Days 1 & 2 Dose- Date started-
2. Prednisolone 60 mg/ m^2 p/o daily Days 3 – 7 Dose - Day 8 Pred Response-
3. Inj Methotrexate IT stat Day 1 Dose- Date-

INDUCTION

Phase I: 2 - 5 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4 (Dose:)(Day 8,- Day15- Day 22- Day 29-
2. Daunorubicin 30 mg/ m^2 iv weekly x 4 (Dose:)(Day 8,- Day15- Day 22- Day 29-
3. L'Asparaginase* 5,000 U/ m^2/day IV every third day X 8 doses (Dose-)

* Leunase to be started 12 hours after VCR. Doses can be rounded up to 10,000 or 5000 IU.

(Day12- Day15- Day18- Day21- Day24- Day27- Day30- Day 33-

4. Prednisolone 60 mg/ m^2 p/o divided in 3 doses x 3 weeks and then taper over 10 days
5. Inj Methotrexate IT stat day 12 Date-

1 week after completion of Phase I, BM and CSF to assess remission status Date-

Phase II: 6 - 9 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 & Day 29 (Dose-)(Day 1- Day 29-
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Days 1 - 4) followed by 3 days rest. (Dose-)
   Repeat x Total 4 cycles of Ara-C

1^{st} cycle : Date from to 3. Intrathecal MTX
2^{nd} cycle :Date from to Dates: 2^{nd} week-
3^{rd} cycle : Date from to
4^{th} cycle : Date from to 4^{th} week-

3. **Intrathecal Methotrexate weekly x 2**
4. 6-Mecapto-purine- 60 mg/m^2, PO for 28 days evening, fasting without milk.
   Dose- Date from- to-

2 WEEKS REST

12 - 20 wks Date of starting: Date of completion:
Date of counts: Date of counts:
1. 6-Mercaptopurine* 50 mg/ m^2 p/o daily x 8 weeks Dose-
2. Methotrexate* 20 mg/ m^2 p/o once a week x 8 weeks Dose-

* in the evening on a fasting stomach without milk. Co-trimoxazole to be taken on Wed & Thu

TWO WEEKS REST

REINDUCTION

Phase I: 23 - 27 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4(Dose:)(Day 1,- Day 8- Day 15- Day 21-)
2. Adriamycin 30 mg/ m^2 iv weekly x 4(Dose:)(Day 1,- Day 8- Day 15- Day 21-)
3. L'Asparaginase* 40,000 U/ m^2 (total) iv given in divided doses of 10,000 U on days 2, 5,9 & 12

* Leunase to be started 12 hours after VCR. Doses can be rounded up to 10,000 or 5000 IU.

(Dose:)(Day 2,- Day 5- Day 9- Day 12-)

4. Dexamethasone 10 mg/ m^2 p/o daily x 4 weeks and then taper over 10 days(Dose-)

Phase II: 28 - 30 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 Dose- (Date-)
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Day 1 - 4) followed by 3 days rest. (Dose-)
   Repeat x Total 2 cycles of Ara-C

1st cycle : Date from to
2nd cycle :Date from to

TWO WEEKS REST

MAINTENANCE

33 - 137 wks Date of starting: Date of completion:

1. 6-Mercaptopurine* 50 mg/ m^2 p/o daily x 2 years (Dose-)
2. Methotrexate* 20 mg/ m^2 p/o once a week x 2 years (Dose-)
3. Inj Vincristine 1.4 mg/m^2 once a month x 2 years (Dose-)
4, Tab Dexa 6 mg/m^2 daily for 5 days once a month x 2 years (Dose-)
5. Inj MTx IT stat once every three months x 2 years (Dose-)

* in the evening on a fasting stomach without milk. Co-trimoxazole to be taken on Wed & Thu

Reference – ALL BFM 1995
Modified May, 2009

Pediatric ALL : PROTOCOL III

Intermediate Risk

NO HDMTX , WITH RADIOTHERAPY

- **Age >6 years**
- **WBC >20,00cmm**
- **T cell immunophenotype (any aberrant markers)**
- **t(1 ;19)**
- **Pro B cell ALL without 11q23.**
- **CNS disease or testicular disease at diagnosis**
- **(+ prednisolone good response + marrow in remission – Post Ph I Induction)**
- **Lower Socio-economic status.**

PREINDUCTION **(1 week)**

1. Dexamethasone 6 mg/ m^2 iv Days 1 & 2 Dose- Date started-.
2. Prednisolone 60 mg/ m^2 p/o daily Days 3 – 7 Dose - Day 8 Pred Response-
3. Inj Methotrexate IT stat Day1. Dose- Date-

INDUCTION

Phase I: 2 - 5 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4 (Dose:)(Day 8,- Day15- Day 22- Day29-)
2. Daunorubicin 30 mg/ m^2 iv weekly x 4(Dose:)(Day 8,- Day15- Day 22- Day29-)
3. L'Asparaginase 105,000 U/ m^2 (total dose) iv given as: (Leunase to be started 12 hours after VCR.)
   - 0.5 m^2 : 5000 U A/D x 10 doses
   - 0.75 m^2 : 10,000 U A/D x 8 doses
   - 1.0 m^2 : 10,000 U A/D x 10 doses

   Doses can be rounded up to 10,000 or 5000 IU.

   (Day 8- Day10- Day12- Day14- Day 16- Day 18- Day 20- Day 22-
4. Prednisolone 60 mg/ m^2 p/o daily x 3 weeks and then taper over 10 days

1 week after completion of Phase I, BM to assess remission status Date-

Phase II: 6 - 9 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 & Day 29 (Dose-)(Day 1- Day 29-)
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Days 1 - 4) followed by 3 days rest. (Dose-)

   Repeat x Total 4 cycles of Ara-C

1st cycle : Date from to
2nd cycle :Date from to
3rd cycle : Date from to
4th cycle : Date from to

CNS PROPHYLAXIS **Given Concurrently with Phase II Induction**

1. Intrathecal Methotrexate weekly x 4 Dates: 1st-
2nd-
3rd-
4th-

2. Cranial RT (No RT < 1 yr) Date of starting: Date of completion:

a. Prophylactic ≥1yr 12 Gy
b. Therapeutic ≥1 yr <2 yr 12 Gy
≥ 2 yr 18 Gy **2 WEEKS REST**

12 - 20 wks Date of starting: Date of completion:
Date of counts: Date of counts:
1. 6-Mercaptopurine* 50 mg/ m^2 p/o daily x 8 weeks Dose-
2. Methotrexate* 20 mg/ m^2 p/o once a week x 8 weeks Dose-

* in the evening on a fasting stomach without milk. Co-trimoxazole to be taken on Wed & Thu

TWO WEEKS REST

REINDUCTION

Phase I: 23 - 27 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4(Dose:)(Day 1,- Day 8- Day 15- Day 21-)
2. Adriamycin 30 mg/ m^2 iv weekly x 4(Dose:)(Day 1,- Day 8- Day 15- Day 21-)
3. L'Asparaginase* 40,000 U/ m^2 (total) iv given in divided doses of 10,000 U on days 2, 5,9 & 12

* Leunase to be started 12 hours after VCR. Doses can be rounded up to 10,000 or 5000 IU.

(Dose:)(Day 2,- Day 5- Day 9- Day 12-)

4. Dexamethasone 10 mg/ m^2 p/o daily x 4 weeks and then taper over 10 days(Dose-)

Phase II: 28 - 30 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 Dose- (Date-)
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Day 1 - 4) followed by 3 days rest. (Dose-)

Repeat x Total 2 cycles of Ara-C

1st cycle : Date from to
2nd cycle :Date from to

TWO WEEKS REST

MAINTENANCE

33 - 137 wks Date of starting: Date of completion:

1. 6-Mercaptopurine* 50 mg/ m^2 p/o daily x 2 years (Dose-)
2. Methotrexate* 20 mg/ m^2 p/o once a week x 2 years (Dose-)
3. Inj Vincristine 1.4 mg/m^2 once a month x 2 years (Dose-)
4, Tab Dexa 6 mg/m^2 daily for 5 days once a month x 2 years (Dose-)
5. Inj MTx IT stat once every three months x 2 years (Dose-)

* in the evening on a fasting stomach without milk. Co-trimoxazole to be taken on Wed & Thu

Reference – ALL BFM 1995
Modified May, 2009

Appendix 3: Standard risk BFM 95

- **Age > 1 yr, < 6 yrs**
- **WBC ≤ 20,000/cmm**
- **Prednisolone good response**
- **Precursor B, CALLA immunophenotype (no T immunophenotype, no aberrant markers)**
- **No translocation t(9;22) or t(4;11)**
- **No CNS disease**
- **Higher Socio-economic status**

PREINDUCTION **(1 week)**

1. Dexamethasone 6 mg/ m^2 iv Days 1 & 2 Dose- Date started-.
2. Prednisolone 60 mg/ m^2 p/o daily Days 3 – 7 Dose - Day 8 Pred Response
3. Inj Methotrexate IT stat Day 1 Dose- Date-

INDUCTION

Phase I: 2 - 5 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4 (Dose:)(Day 8,- Day15- Day 22- Day 29-
2. Daunorubicin 30 mg/ m^2 iv weekly x 2 (Dose:)(Day 8- Day15-)
3. L'Asparaginase* 5,000 U/ m^2/day IV every third day X 8 doses (Dose-)

* Leunase to be started 12 hours after VCR. Doses can be rounded up to 10,000 or 5000 IU.

(Day12- Day15- Day18- Day21- Day24- Day27- Day30- Day 33-

4. Prednisolone 60 mg/ m^2 p/o divided in 3 doses x 3 weeks and then taper over 10 days
5. Inj Methotrexate IT stat day 12 Date-

1 week after completion of Phase I, BM and CSF to assess remission status Date-

Phase II: 6 - 9 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 & Day 29 (Dose-)(Day 1- Day 29-
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Days 1 - 4) followed by 3 days rest. (Dose-)
   Repeat x Total 4 cycles of Ara-C

1^{st} cycle : Date from to 3. Intrathecal MTX
2^{nd} cycle :Date from to Dates: 2^{nd} week-
3^{rd} cycle : Date from to
4^{th} cycle : Date from to 4^{th} week-

3. **Intrathecal Methotrexate weekly x 2**
4. 6-Mecapto-purine- 60 mg/m^2, PO for 28 days evening, fasting without milk.
   Dose- Date from- to-

2 WEEKS REST

CONSOLIDATION THERAPY

12 - 20 wks -Medium Dose Methotrexate-(See Protocol)

1. MP: 6-Mercaptopurine- 25 mg/m2/d, PO, day: 1 – 56, Dose- in the evening on a fasting stomach without milk.

2. MD MTX: Medium-dose methotrexate- 2,000 mg/m2/d, PI, over 24 h, q 14 days (x 4) on day: 8, 22, 36, 50.

- 1/10 of the total dose (200 mg/m2) should be administered PI over 30 minutes as a loading dose.
- 9/10 of the total dose (1,800 mg/m2) is to be given PI over 23.5 h.

3. LCV-Rescue-15 mg/m2 i.v. x 3 at h: +42, +48, +54

4. MTX IT: Intrathecal methotrexate 1 h after the start of MTX infusion.

a. <1yr 6 mg b. 1 - 2yr 8 mg
c. 2 - 3yr 10 mg d. >3yr 12 mg

TWO WEEKS REST

REINDUCTION

Phase I: 23 - 27 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4 (Dose:)(Day 8,- Day 15- Day 22- Day 29-
2. Adriamycin 30 mg/ m^2 iv over 1 hour , weekly x 4 (Dose:)(Day 8,- Day 15- Day 22- Day29
3. L'Asparaginase* 10,000 U/ m^2 /dose iv/im/sc given 10,000 U x 4 doses

* Leunase to be started 12 hours after VCR. Doses can be rounded up to 10,000 or 5000 IU.

(Dose:)(Day 9,- Day 12- Day 16- Day 19-)

4. Dexamethasone 10 mg/ m^2 p/o daily in 3 divided doses x 4 weeks and then taper over 10 days..

Phase II: 28 - 30 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 (Dose-)(Date-)
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Day 1 - 4) followed by 3 days rest.
   Repeat x Total 2 cycles of Ara-C (Dose-)

1^{st} cycle : Date from to
2^{nd} cycle :Date from to

3. 6 TG- 60 mg/m^2 PO,
4. Inj MTx IT stat day 1 and day 8(Dose:)(Day 1- Day 8 -)

TWO WEEKS REST

FINAL MAINTENANCE

33 - 137 wks Date of starting: Date of completion:

1. 6-Mercaptopurine* 50 mg/ m^2 p/o daily x 2 years (Dose-)
2. Methotrexate* 20 mg/ m^2 p/o once a week on Sunday x 2 years (Dose-)
3. Inj. Methotrexate IT every monthly x 4 doses from 2^{nd} month

Dose- 2^{nd} month- 4^{th} month-
3^{rd} month- 5^{th} month-

* in the evening on a fasting stomach without milk. Co-trimoxazole to be taken on Wed & Thu

Ref erence: ALL IC BFM 2002

Modified May, 2009

Appendix 4: Standard risk
Non Methotrexate/No radiation based study protocol

- **Age > 1 yr, < 6 yrs**
- **WBC ≤ 20,000/cmm**
- **Prednisolone good response**
- **Pre B, CALLA immunophenotype (no T immunophenotype, no aberrant markers)**
- **No translocation t(9;22) or t(4;11)**
- **No CNS disease**

PREINDUCTION **(1 week)**

1. Dexamethasone 6 mg/ m^2 iv Days 1 & 2
2. Prednisolone 60 mg/ m^2 p/o daily Days 3 - 7
3. Inj Methotrexate IT stat Day 1

INDUCTION

Phase I: 2 - 5 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4 (Day 8,15,22,29)
2. Daunorubicin 30 mg/ m^2 iv weekly x 2 (Day 8,15)
3. L'Asparaginase 5,000 U/ m^2/day IV every third day X 8 doses (days12,15,18,21,24,27,30,33) (minimum number of doses=8)
4. Prednisolone 60 mg/ m^2 p/o daily x 3 weeks and then taper over 10 days
5. Inj Methotrexate IT stat day 15

1 week after completion of Phase I, BM and CSF to assess remission status

Phase II: 6 - 9 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1 & Day 29
2. AraC 75 mg/ m^2 iv/sc daily x 4 days (Days 1 - 4) followed by 3 days rest. Repeat x Total 4 cycles of Ara-C
3. **Intrathecal Methotrexate weekly x 4**

a. <1yr 6 mg b. 1 - 2yr 8 mg

c. 2 - 3yr 10 mg d. >3yr 12 mg

NO CRANIAL PROPHYLAXIS
2 WEEKS REST

INTERIM MAINTENANCE

12 - 20 wks

1. 6-Mercaptopurine 50 mg/ m^2 p/o daily x 8 weeks
2. Methotrexate 20 mg/ m^2 p/o once a week x 8 weeks
3. Inj MTx IT at day 28 – single dose

TWO WEEKS REST

REINDUCTION

Phase I: 23 - 27 wks

1. Vincristine 1.5 mg/ m^2 iv weekly x 4
2. Adriamycin 30 mg/ m^2 iv weekly x 4
3. L'Asparaginase 10,000 U/ m^2 /dose iv/im/sc given 10,000 U on days 1, 4, 7 & 11
4. Dexamethasone 10 mg/ m^2 p/o daily x 4 weeks and then taper over 10 days
5. Inj MTx IT stat day 1 and day 18

Phase II: 28 - 30 wks

1. Cyclophosphamide 1000 mg/ m^2 iv Day 1
2. Ara C 75 mg/ m^2 iv/sc daily x 4 days (Day 1 - 4) followed by 3 days rest.
   Repeat x Total 2 cycles of Ara-C

TWO WEEKS REST

MAINTAINENCE :

33 - 137 wks

1. 6-Mercaptopurine 50 mg/ m^2 p/o daily x 2 years (2 1/2 years for boys)
2. Methotrexate 20 mg/ m^2 p/o once a week x 2 years (2 1/2 years for boys)
3. Inj Vincristine 1.4 mg/m^2 once a month x 2 years (2 1/2 years for boys)
4, Tab Dexa 6 mg/m^2 daily for 5 days once a month x 2 years(2 1/2 years for boys)
5. Inj MTx IT stat once every three months x 2 years (2 1/2 years for boys)

Hospital No	NAME	AGE	SEX	Year	ate of Diagnos	Liversize	Spleensize	CNS	CNSStage	eural Effusi	Testis	WBC	M Bla	IPT Status	IPT	N diagnosis	RTPCR	BCR_ABL	TEL_AML	MLL_AF4	E2A / PBX	Cytogenetic	CTG Ris	Risk group	Status at Sta	Treatment Taken	Protocols	Induction start	Relapse	Date of Relapse	Date of death	use of dea	
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200892F	Hemanth	15	1	2012	5-23-2012	0	0	2	1	2	2	2.3	84	1	1	2	1	2	2	2	2	7,9)(p11-	3	1	1	1	5	5-23-2012	2		6-18-2012	2	
132370F	Nayana C P	16	2	2012	2-7-2012	0	0	2	1	2	3	8.9	96	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1	1	5	2-15-2012	2				5
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140271F	Prosenjit Barua	18	1	2012	2-27-2012	0	0	2	1	2	2	2	85	1	3	2	2	2	2	2	2	6,3q44),del(4)	3	1	1	1	5	2-29-2012	2				5
211660F	Dhana Lakshmi A	18	2	2012	5-30-2012	3	0	1	3	2	3	103.1	90	1	1	2	1	2	2	2	2	NO	4	3	1	1	5	5-31-2012	2				5
227665F	Harsha S K	20	1	2012	6-23-2012	0	3	2	1	2	2	6.4	100	1	1	2	1	2	2	2	2	22 or	5	1	1	1	5	6-30-2012	2				5
212165F	Ramya G	23	2	2012	5-29-2012	0	0	2	1	2	3	1.2	98	1	1	2	1	2	2	2	2	13q25)[4]/46,	5	1	1	1	5	6-15-2012	1	10-29-2012	12-29-2012	2	
148051F	Mohammad Mozaffar Hossain	24	1	2012	3-21-2012	0	0	2	1	2	2	9.5	82	1	3	2	2	2	2	2	2	46,XY[19]	5	1	1	1	5	3-28-2012	1	7-20-2012	8-17-2012	1	
227813F	Karthikeyan D	24	1	2012	6-30-2012	0	0	2	1	2	2	6.2	0	1	1	2	1	2	2	2	1	11.2),der(9)(9	2	1	1	1	5	7-10-2012	1	12-10-2013	2-22-2014	1	
193051F	Sampa Baidya	25	2	2012	5-12-2012	0	0	2	1	2	3	2.9	7	1	1	2	1	2	2	2	2	46,XX[10]	5	1	1	1	5	5-23-2012	1	11-14-2012	12-13-2012	1	
226809F	Vatturi Subbarao	25	1	2012	6-16-2012	0	0	2	1	2	2	3	94	1	1	2	1	1	2	2	2	9,t(9;22)(q34;	3	3	1	1	5	6-25-2012	2		9-3-2012	1	
211604F	Gowtham Kumar B	26	1	2012	5-31-2012	0	0	2	1	2	2	13.8	98	1	1	2	1	2	2	2	2	46,XY[1cell]	1	1	1	1	5	6-9-2012	1	10-5-2012	2-25-2013	1	
211928F	Rajabharathi	31	1	2012	6-2-2012	0	0	1	3	1	2	531.4	87	1	3	2	1	2	2	2	2	6)(q21q24),-	3	3	1	1	5	6-9-2012	2				5
112643F	Subbiah M	34	1	2012	1-18-2012	3	4	1	3	2	2	5.4	96	1	1	2	1	2	2	2	2	46,XY[12]	5	1	1	1	5	1-26-2012	2		9-23-2012	2	
130839F	Thilagar Babick Kumar	35	1	2012	2-9-2012	0	0	2	1	2	2	96.8	88	1	1	2	1	2	2	2	2	21)[13]/46,XY[	5	3	1	1	5	2-18-2012	1	6-25-2013	6-25-2013	1	
193196F	Senthil Kumar S	36	1	2012	4-30-2012	0	6	1	3	2	2	27.1	80	1	1	2	1	2	2	2	2	21 or	5	3	1	1	5	5-9-2012	1	9-28-2012	10-28-2012	1	
133359F	Basi K K	45	1	2012	2-13-2012	0	0	2	1	2	2	5.8	46	1	1	2	1	2	2	2	2	ns(9;?)(p13;?)	3	3	1	1	5	2-22-2012	2				5
038021F	Rakesh Kumar	15	1	2011	9-22-2011	0	0	2	1	2	2	72	30	1	3	2	2	2	2	2	2	Y,der(9)t(9;?	3	1	1	1	5	9-22-2011	2				5
073314F	Twinkle Kumari	15	2	2011	11-14-2011	2	2	2	1	2	3	2.6	100	1	1	2	1	2	1	2	2	16,+mar?der(	3	1	1	1	5	11-14-2011	2				5
853124D	Prabhu M	15	1	2011	1-6-2011	2	0	1	3	2	2	0.8	93	1	1	2	1	2	2	2	2	2)(p11-12;p11-	1	1	1	1	5	1-6-2011	2				5
870875D	Rishabh Singh	15	1	2011	2-9-2011	1	0	2	1	2	2	1.2	92	1	1	2	1	2	2	2	2	46,XY[19]	5	1	1	1	5	2-9-2011	2				5
877055D	Neeraj Kumar	15	1	2011	2-4-2011	2	0	2	1	2	2	1.2	90	1	3	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	2-14-2011	2				5
928509D	Tanu Dey	15	2	2011	4-27-2011	0	0	2	1	2	3	4.1	20	1	1	2	1	2	2	2	2	1,+2,+4,+5,+6	1	1	1	1	5	5-4-2011	1	10-11-2011	11-11-2011	1	
003214F	Stephen G	16	1	2011	8-19-2011	4	10	2	1	2	2	11	52	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	8-19-2011	2				5
916739D	Baskar B	16	1	2011	4-18-2011	0	0	2	1	2	2	2.4	98	1	1	2	1	2	2	2	2	INCOMPLET	4	1	1	1	5	4-19-2011	2		5-15-2011	2	
935653D	Divaya Bharathi L	16	2	2011	6-4-2011	4	0	2	1	2	3	13.3	95	1	1	2	1	1	2	2	2	28),t(9;22)(q3	3	3	1	1	5	6-13-2011	1	10-21-2011	11-21-2011	1	
975363D	Abdul Ajeez	16	1	2011	7-12-2011	5	2	2	1	2	2	2	96	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	7-21-2011	2				5
006024F	Wazda Tabasshum	17	2	2011	9-7-2011	3	0	1	3	2	3	37.8	85.5	1	3	2	2	2	2	2	2	(p22;?),t(14;1	3	1	1	1	5	9-10-2011	2				5
007357F	Archana Kumari	17	2	2011	8-13-2011	5	3	2	1	2	3	4.6	86	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1	1	5	9-12-2011	2				5
916312D	Ankaiah Anthony V	17	1	2011	4-2-2011	0	0	1	3	2	2	15.2	82	1	2	2	1	2	2	2	2	+der(1)t(4;?	1	1	1	1	5	4-2-2011	1	7-20-2012	2-11-2013	1	
939190D	Lavanya Priya M	17	2	2011	5-12-2011	0	0	2	1	2	3	63.3	79	1	3	2	1	2	2	2	2	q36;q13)[7]/4	5	3	1	1	5	5-13-2011	2				5
948459D	Asasur Sardar	17	1	2011	5-23-2011	0	4	2	1	2	2	89.8	98	1	1	2	1	2	2	2	2	46,XY[20]	5	3	1	1	5	6-1-2011	2				5
994380D	Saheb Hossain	17	1	2011	7-27-2011	3	4	2	1	2	2	4.8	93	1	1	2	1	2	2	2	2	31),dic(9;12)(	1	1	1	1	5	7-28-2011	2				5
085328F	Suhail K	18	1	2011	12-3-2011	6	8	2	1	2	2	1.4	100	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	12-15-2011	2				5
880586D	Allen	18	1	2011	2-11-2011	4	5	1	3	2	2	183.4	97	1	3	2	2	2	2	2	2	)[p13;q11][18]	5	3	1	1	5	2-19-2011	1	12-31-2011	1-30-2012	1	
966711D	Shaik Sharuddin	18	1	2011	6-24-2011	5	9	2	1	2	2	185.4	96	1	1	2	1	2	2	2	2	PARTIAL A	5	3	1	1	5	7-1-2011	2				5
982305D	Ramaswamy S	18	1	2011	7-12-2011	4	0	1	3	2	2	12.7	61	1	3	2	2	2	2	2	2	del(6)(q13),del	3	1	1	1	5	7-21-2011	2				5
985265D	Gopal Mandal	18	1	2011	8-20-2011	4	6	2	1	2	2	173.3	85	1	1	2	1	2	2	2	2	Not Done	4	3	1	1	5	8-22-2011	2				5
046087F	Harikrishnan V	19	1	2011	10-11-2011	2	3	2	1	2	2	424.5	80	1	3	2	2	2	2	2	2	46,XY[20]	5	3	1	1	5	10-13-2011	1	3-20-2012	4-20-2012	1	
868827D	Khairul Mandal	19	1	2011	2-4-2011	0	3	2	1	2	2	9.7	54	1	1	2	1	1	2	2	2	46,XY[20]	5	3	1	1	5	2-4-2011	2				5
959678D	Thendral	19	2	2011	6-18-2011	0	0	2	1	2	3	41.6	85	1	1	2	1	2	2	2	2	+ins(4;?)(q?2	1	3	1	1	5	6-27-2011	2				5
653058B	Geetha	23	2	2011	2-18-2011	2	0	2	1	2	3	9.5	45	1	1	2	1	1	2	2	2	q34;q11.2)[13	3	3	1	1	5	3-25-2011	1	9-24-2012	10-24-2012	1	
937829D	Sarwath Nashrin	23	2	2011	5-24-2011	2	0	2	1	2	3	3.9	70	1	1	2	1	2	2	2	2	Not Done	4	1	1	1	5	6-6-2011	2				5
969645D	Jiten Majhi	24	1	2011	7-22-2011	4	2	2	1	2	2	2.7	90	1	3	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	7-25-2011	1	6-25-2012	7-29-2012	1	
055934F	Prashanth Patil	26	1	2011	10-19-2011	2	2	2	1	2	2	3.8	92	1	3	2	2	2	2	2	2	)(p15)[3]/46,	5	1	1	1	5	10-27-2011	2				5
105524F	Kumar S	26	1	2011	12-31-2011	0	0	2	1	2	2	45	100	1	1	2	1	2	2	2	2	Not Done	4	3	1	1	5	1-3-2012	2		2-18-2012	2	
842302D	Plyrishaw	28	1	2011	1-5-2011	6	15	2	1	1	2	67.3	76	1	3	2	1	2	2	2	2	46,XY[6]	5	3	1	1	5	1-20-2011	2				5
977460D	Sakeer V K	28	1	2011	7-2-2011	0	0	2	1	2	2	2.5	70	1	1	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	7-14-2011	2				5

983639D	Riswan Babu	28	1	2011	7-19-2011	0	0	2	1	2	2	16.5	93	1	3	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	7-29-2011	2			5
064391B	Sisodiya Chandra Bose	29	1	2011	2-3-2011	4	0	2	1	2	2	1.9	35	1	3	2	2	2	2	2	2	2	46,XY,del(12)(p	5	1	1	1	5	2-15-2011	2			5
054166F	Kandaswamy A	31	1	2011	10-20-2011	0	0	2	1	2	2	6.9	86	1	1	2	1	2	2	2	2	2	46,XY[20]	5	1	1	1	5	10-20-2011	2		11-2-2011	2
884016D	Govindaraj	33	1	2011	7-28-2011	4	0	2	1	2	2	331.6	91	1	3	2	2	2	2	2	2	2	46,XY[7]	5	3	1	1	5	7-28-2011	2			5
902811D	Shailesh Sidhanshu Topnu	35	1	2011	3-15-2011	4	5	2	1	2	2	1.7	5	1	1	2	1	1	2	2	2	2	46,XY[20]	5	3	1	1	5	3-21-2011	2			5
967339D	Ramesh T	35	1	2011	6-18-2011	4	0	1	3	2	2	56.4	85	1	3	2	2	2	2	2	2	2	Not Done	4	5	1	1	5	6-25-2011	2			5
032661F	Papathi P	36	2	2011	9-27-2011	3	0	2	1	2	3	2.7	32	1	1	2	1	2	2	2	2	2	Not Done	4	1	1	1	5	10-6-2011	2			5
009141F	Suman Devi	37	2	2011	8-20-2011	0	0	2	1	2	3	30	98	1	3	2	2	2	2	2	2	2	46,XX[18]	1	1	1	1	5	8-25-2011	2			5
028511F	Sabareeswaran N	37	1	2011	9-17-2011	2	0	2	1	2	2	0.7	72	1	1	2	1	2	2	2	2	2	47,XY,+mar[2]/4	1	5	1	1	5	9-18-2011	1	3-22-2012	9-7-2012	1
010989F	Sim Sumith Mathew	38	1	2011	12-2-2011	0	0	1	3	2	2	10.5	0	1	1	2	1	2	2	2	2	2	46,XY[20]	5	5	1	1	5	12-12-2011	2			5
875161D	Dilshad S K	38	2	2011	2-10-2011	0	0	2	1	2	3	9.9	95	1	1	2	1	2	2	2	2	2	46,XX,del(X)(q276	3	5	1	1	5	2-20-2011	2		4-30-2011	2
484022A	Mary Bernadath	41	2	2011	12-27-2011	0	0	2	1	2	3	2.2	85	1	1	2	1	2	2	2	2	2	92,XX,+1,+2,-3,+4,-	3	5	1	1	5	1-6-2012	2		2-10-2012	2
103646F	Uma Maheswari	42	2	2011	12-28-2011	0	5	2	1	2	2	234	85	1	1	2	1	1	2	2	2	2	5,add(5)(q35),	3	3	1	1	5	1-7-2012	2		5-13-2012	1
920204D	Boopalan A	43	1	2011	4-9-2011	0	0	2	1	2	2	59.2	90	1	3	2	2	2	2	2	2	2	q14q21),	3	5	1	1	5	4-9-2011	2		5-1-2011	2
889589D	Kisan Dagdu Sawant	45	1	2011	2-24-2011	0	0	2	1	2	2	6.2	85	1	1	2	1	2	2	2	1	2	t(1;19)(q23;p1	2	1	1	1	5	3-5-2011	2			5
007966F	Gangadaran S	48	1	2011	8-19-2011	0	0	2	1	2	2	7.6	61	1	3	2	1	2	2	2	2	2	46,XY[20]	5	5	1	1	5	8-20-2011	2			5
870742D	Anbuselvi Venkatar	49	2	2011	1-25-2011	0	2	2	1	2	3	47.1	90	1	1	2	1	1	2	2	2	2	2)(p11-	3	3	1	1	5	1-27-2011	2			5
901281C	Satyanarayana V	52	1	2011	5-27-2011	2	0	1	3	2	2	4.5	65	1	1	2	1	2	2	2	2	2	Y,+1,+1,-3,-	3	1	1	1	5	6-6-2011	2		2-7-2012	2
911125D	Dharmaraj C	55	1	2011	3-29-2011	0	0	2	1	2	2	1.6	90	1	1	2	1	2	2	2	2	2	der(3)?inv(3)(	1	5	1	1	5	4-15-2011	2			5
043658B	Mahaveer Kumar J	56	1	2011	6-20-2011	0	0	2	1	2	2	284.6	90	1	1	2	1	1	2	2	2	2	(1)(p36)	3	3	1	1	5	6-20-2011	1	9-4-2012	9-16-2012	1
674005D	Daniel S	15	1	2010	4-10-2010	0	0	2	1	2	2	7	60	1	3	2	2	2	2	2	2	2	7)(q36) cr	3	1	1	1	5	4-13-2010	2			5
653650D	Khanapuram Kharumnuid	16	1	2010	3-15-2010	3	6	2	1	1	2	1	58	1	2	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	3-15-2010	1	5-14-2010	5-27-2010	1
660814D	Raghvender Sahdev	16	1	2010	3-20-2010	0	3	2	1	2	2	40	89	1	3	2	2	2	2	2	2	2	31),der(17)?h	5	1	1	1	5	3-20-2010	2			5
669532D	Shiv Kumar Jha	16	1	2010	4-3-2010	0	0	2	1	1	2	11	46	1	3	2	2	2	2	2	2	2	Not Done	4	1	1	1	5	4-13-2010	1	3-29-2011	5-26-2011	1
749393D	Aishwarya Jha	16	2	2010	8-3-2010	4	0	2	1	2	3	14.7	80	1	3	2	2	2	2	2	2	2	46,XX[20]	5	3	1	1	5	8-12-2010	2			5
804498D	Sheik Karam	16	1	2010	10-29-2010	0	4	2	1	2	2	1177	84	1	3	2	2	2	2	2	2	2	4,i(7)(q10),+2	5	5	1	1	5	10-31-2010	1	9-13-2011	6-18-2012	1
824119D	Deepti Barman	16	2	2010	11-10-2010	0	0	2	1	2	3	25.4	94.5	1	1	2	1	2	2	2	2	2	46,XX[20]	5	1	1	1	5	11-18-2010	2		12-22-2010	2
619627D	Kiranraj R	17	1	2010	1-15-2010	3	2	2	1	2	2	3.2	78	1	1	2	1	2	2	2	2	2	46,XY[20]	5	1	1	1	5	1-23-2010	1	8-9-2011	1-22-2012	1
686590D	Pandivel S.	17	1	2010	5-6-2010	6	6	2	1	2	2	12	92	1	3	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	5-13-2010	2			5
696967D	Rishfan Nazeer	17	1	2010	5-13-2010	2	0	2	1	2	2	0.8	96	1	1	2	1	2	2	2	2	2	46,XY[20]	5	1	1	1	5	5-16-2010	2			5
753306D	Balaji K	17	1	2010	8-7-2010	4	2	1	3	2	2	92.4	91	1	1	2	1	2	2	2	2	2	p21),add(20)(	5	1	1	1	5	8-14-2010	2			5
834821D	Mohammed Ajmal K V	17	1	2010	11-26-2010	2	0	2	1	2	2	9.1	38	1	1	2	1	2	2	2	2	2	+Y,+1,+2,+4,+	1	1	1	1	5	11-29-2010	2			5
630085D	Revathi A.	18	2	2010	2-6-2010	2	1	2	1	2	3	9.1	24	1	1	2	1	2	2	2	2	2	46,XX[20]	5	1	1	1	5	3-2-2010	1	10-28-2011	4-16-2012	1
702166D	Libin Louis	18	1	2010	5-21-2010	3	3	2	1	2	2	47.6	40	1	1	2	1	2	2	2	2	2	q31;q275),i(8)	3	3	1	1	5	5-28-2010	2		7-28-2010	1
716927D	Sajed Khan	18	1	2010	6-26-2010	0	0	2	1	2	2	3	88	2	5	2	2	2	2	2	2	2	q13q33),i(8)(q	5	1	1	1	5	7-13-2010	2			5
775888D	Dilip Kumar	18	1	2010	9-6-2010	0	0	2	1	2	2	7	4	1	3	2	2	2	2	2	2	2	Not Done	4	5	1	1	5	9-18-2010	1	3-1-2011	4-29-2011	1
804282D	Kumaresan	18	1	2010	10-28-2010	3	3	2	1	2	2	25	0	1	3	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	10-28-2010	2			5
830320D	Vineet Jose	18	1	2010	11-18-2010	0	0	2	1	2	2	12	77	1	3	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	11-25-2010	2		11-30-2010	2
853388D	Ethiraj A	19	1	2010	12-30-2010	3	0	2	1	2	2	28	93	1	3	2	2	2	2	2	2	2	q22;[10]/46,X	5	1	1	1	5	12-30-2010	2			5
623429D	Mushabheer	20	1	2010	1-22-2010	0	0	2	1	2	2	0.7	98	1	1	2	1	2	2	2	2	2	][14]/46,XY[8]	5	1	1	1	5	1-23-2010	2			5
848206D	Gyendey Zam	20	2	2010	12-17-2010	0	0	1	3	2	3	198	90	1	3	2	2	2	2	2	2	2	7,add(14)(q32	3	5	1	1	5	12-17-2010	2		2-11-2011	1
703362D	Aswini M P	21	2	2010	5-22-2010	0	0	1	3	2	3	182	98	1	1	2	1	2	2	2	2	2	47,XX,+8[20]	5	5	1	1	5	5-30-2010	2			5
627089D	Mohammed Zahir Ekbal	22	1	2010	1-29-2010	0	0	2	1	2	2	7.2	44	1	1	2	1	2	2	2	2	2	Y,+del(4)(q22	3	1	1	1	5	1-29-2010	1	7-17-2010	11-7-2010	1
661054D	Senthil Kumar R	23	1	2010	3-24-2010	6	0	2	1	1	2	90	75	1	3	2	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	3-31-2010	2			5
691558D	Tania Ahmed	23	2	2010	5-13-2010	2	0	2	1	2	3	8.2	40	1	1	2	1	2	2	2	2	2	q21q22)[2]/46	5	1	1	1	5	5-16-2010	1	6-1-2013	7-3-2013	1
797650D	Vinu T Thottumkal	23	1	2010	10-1-2010	0	2	2	1	2	2	9	80	1	1	2	2	2	2	2	2	2	Y[7]/45,idem,d	5	1	1	1	5	10-22-2010	2			5
815053D	Savithri Devi	25	2	2010	11-17-2010	3	0	2	1	2	3	71	82	1	1	2	1	2	2	2	2	2	46,XX[20]	5	3	1	1	5	11-30-2010	2		4-4-2011	1
837278D	Arul Shanthi S	25	2	2010	12-11-2010	0	0	2	1	2	3	26.9	74	1	1	2	1	2	2	2	2	2	1;6)(q27?13;q	1	1	1	1	5	12-24-2010	2		1-12-2011	2
827333D	Lakshmi E	26	2	2010	11-15-2010	4	0	2	1	2	3	9.4	98	1	1	2	1	2	2	2	2	2	29;q14),del(9)	5	1	1	1	5	11-19-2010	1	7-2-2011	9-19-2011	1
651443D	Kuber Sampath P	27	1	2010	3-12-2010	0	1	2	1	2	2	7.2	74	1	1	2	1	2	2	2	2	2	AMP21[3]/46,	3	1	1	1	5	3-14-2010	2			5
772434D	Akila Kailasam	29	2	2010	9-17-2010	0	4	2	1	2	3	2.2	85	1	2	2	1	2	2	1	2	2	(q21;q23)[6]/4	3	3	1	1	5	10-18-2010	1	3-4-2011	4-10-2011	1
680166D	Nandita Roy	30	2	2010	4-23-2010	0	0	2	1	2	3	146	65	1	3	2	2	2	2	2	2	2	46,XX[20]	5	5	1	1	5	4-30-2010	1	5-14-2011	6-16-2011	1
753331D	Vijayalakshmi G	32	2	2010	8-9-2010	0	0	2	1	2	3	48	92	1	3	2	2	2	2	2	2	2	46,XX[20]	5	1	1	1	5	8-17-2010	2			5
749160D	Sahidul Hoque	39	1	2010	8-9-2010	8	8	2	1	1	2	322	60	1	3	2	2	2	2	2	2	2	(p13)[16]/46,X	5	1	1	1	5	8-14-2010	2			5

742455D	Tapan Karmakar	40	1	2010	7-27-2010	5	0	1	3	2	2	20.7	76	1	1	2	1	2	2	2	2	46,XY[20]	5	3	1	1	5	7-30-2010	2			5
748390D	Mazahar Rahman MD	42	1	2010	8-7-2010	0	0	2	1	2	2	2.5	75	1	1	2	1	2	2	2	2	46,XY[20]	5		1	1	5	8-21-2010	2			5
785376D	Kalaiarasi R.	42	2	2010	9-16-2010	0	0	2	1	2	3	4.2	42	1	1	2	1	1	2	2	2	X,+5,+8,t(9;22	3	3	1	1	5	9-27-2010	2			5
037484C	Usha Rani	50	2	2010	9-18-2010	0	0	2	1	2	3	1.8	13	1	1	2	1	1	2	2	2	X,+1,-2,-3,-4,-	3	3	1	1	5	9-27-2010	1	1-31-2011	7-7-2011	1
613352D	Gowri. N	50	2	2010	2-17-2010	0	0	2	1	2	3	15.9	75	1	1	2	1	2	2	2	2	46,XX[16]	5		1	1	5	2-28-2010	1	10-15-2010	12-9-2010	1
711143D	Johnson T	50	1	2010	6-10-2010	0	0	2	1	2	2	17	0	1	3	2	2	2	2	2	2	Not To Process	4		1	1	5	6-15-2010	2			5
806793D	Iva Saha	50	2	2010	10-20-2010	1	3	2	1	2	3	19.4	87	1	1	2	1	2	2	2	2	t(18;20)(q11.2	5	1	1	1	5	10-23-2010	1	3-17-2011	4-25-2011	1
639300D	Aminamma Isaac Siddique	51	1	2010	2-20-2010	1	0	1	3	2	2	4.4	0	1	1	2	1	2	2	2	2	46,XY[4]	5		1	1	5	3-24-2010	1	9-29-2012	11-2-2012	1
701388D	Sundaram Sankar	55	1	2010	5-19-2010	0	0	2	1	2	2	1.3	90	1	1	2	1	2	2	2	2	46,XY[9]	5		1	1	5	5-29-2010	2			5
653644D	Radha Chellaiah	60	2	2010	3-22-2010	0	0	2	1	2	3	1.1	45	1	1	2	2	2	2	2	2	46,XX[20]	5		1	1	5	3-26-2010	2			5
694174D	Chenniappan	62	2	2010	5-8-2010	0	0	2	1	2	3	6.5	94	1	1	2	1	2	2	2	2	10,del(13)(q1	1		1	1	5	5-10-2010	2			5
448339D	Sheik Hossain Ali	15	1	2009	4-22-2009	0	0	2	1	2	2	51.3	91	1	1	2	1	2	2	2	2	13;q3273)[18]	5	1	1	1	5	5-7-2009	1	6-25-2010	7-21-2010	1
384699D	Ananu Adhikari	16	1	2009	1-6-2009	4	5	2	1	2	2	4.9	28	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	3-14-2009	1	6-19-2009	7-23-2009	1
460607D	Sathish K G	16	1	2009	5-18-2009	4	8	2	1	2	2	6.3	95	1	1	2	1	2	2	2	2	21q24),del(9)(	3	1	1	1	5	5-25-2009	2			5
494191D	Seelaa Reddy Reddy	16	1	2009	7-11-2009	2	2	1	3	1	2	392	90	1	3	2	2	2	2	2	2	(q13.4),7del(1	5		1	1	5	7-22-2009	1	11-3-2009	3-4-2010	1
508176D	Banumathi	16	2	2009	7-28-2009	2	0	1	3	2	3	10	90	1	1	2	1	2	2	2	2	(4)(p16),add(5	3	1	1	1	5	8-8-2009	2			5
508738D	Geetha	16	2	2009	7-29-2009	0	0	2	1	2	3	414	83	1	1	2	1	2	2	2	2	)(q22;p13 or	3		1	1	5	8-5-2009	1	12-22-2009	4-15-2010	1
533838D	Pawan Kumar	16	1	2009	9-4-2009	4	1	2	1	2	2	11.3	87	1	1	2	1	2	2	2	2	trp(1)(q21q32)	1	1	1	1	5	9-19-2009	2			5
395023D	Najumudeen K.	17	1	2009	1-22-2009	0	3	1	3	2	2	154	76	1	3	2	1	2	2	2	2	46,XY[20]	5		1	1	5	1-29-2009	2			5
540551D	Prasad C	17	1	2009	9-12-2009	3	1	1	3	2	2	94.4	94.5	1	3	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	9-21-2009	2			5
447792D	Mincy Domnic	20	2	2009	4-22-2009	2	3	2	1	2	3	6.8	22	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1	1	5	4-24-2009	2			5
486479D	Phanindra Sai I	21	1	2009	6-23-2009	1	3	2	1	2	2	16.1	86	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	7-2-2009	2			5
538592D	Nirmala Elizabeth Mathew	22	2	2009	9-10-2009	1	1	1	3	2	3	8.4	80	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1	1	5	9-19-2009	2			5
591327D	Rajakumari R	22	2	2009	12-2-2009	2	5	2	1	2	3	174.4	92	1	1	2	1	2	2	2	2	9,idem,+9,+22	1	1	1	1	5	12-3-2009	1	10-12-2010	2-21-2011	1
570485D	Pampi Ghosh	23	2	2009	10-26-2009	0	0	2	1	2	3	9	69	1	1	2	1	2	2	2	2	46,XX[12]	5	1	1	1	5	11-5-2009	2			5
594955D	Arun P. John	23	1	2009	12-2-2009	0	0	2	1	2	2	158	70	1	2	2	2	2	2	2	2	11)(q14;p15),-	3		1	1	5	12-2-2009	2			5
382750D	James Tamang	24	1	2009	1-6-2009	0	0	2	1	2	2	1	60	1	3	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	1-18-2009	1	3-18-2009	4-24-2010	1
530199D	Kiruba Sankar	25	2	2009	8-31-2009	2	0	1	3	2	3	1.7	16	1	1	2	1	2	2	2	2	11)(q21;q21;q	3	1	1	1	5	9-10-2009	2			5
424339D	Celiya K.P	26	2	2009	3-13-2009	0	0	2	1	1	3	8	40	1	3	2	2	2	2	2	2	Process	4	1	1	1	5	3-19-2009	2			5
506511D	Hameena Sulfiqer	26	2	2009	7-22-2009	1	1	1	3	2	3	13.9	0	1	1	2	1	2	2	2	2	Not Done	4	1	1	1	5	8-5-2009	2			5
555222D	Nalira K.	26	2	2009	10-8-2009	2	2	2	1	2	3	4.9	3	1	1	2	1	2	2	2	2	15)(2)46,XX[	5	1	1	1	5	10-24-2009	2			5
391576D	Hemagiri	28	1	2009	1-17-2009	0	0	2	1	2	2	1.9	12	1	1	2	1	2	2	2	2	46,XY[2]	5	1	1	1	5	1-28-2009	2			5
429142D	Radha R	28	2	2009	3-24-2009	6	2	2	1	2	3	186	93	1	1	2	1	2	2	2	2	21q24),der(19	2	1	1	1	5	3-31-2009	2			5
475712D	Bikash Rui Das	28	1	2009	6-8-2009	0	0	2	1	2	2	46	83	1	3	2	2	2	2	2	2	add(3)(p25)[8]	5	1	1	1	5	6-18-2009	1	12-16-2011	1-23-2012	1
519119D	Tapas Patra	32	1	2009	8-24-2009	3	3	2	1	2	2	11.9	21	1	1	2	1	1	2	2	2	46,XY[20]	5	3	1	1	5	8-24-2009	2			5
442618D	Mallikarjuna A.J.	33	1	2009	4-11-2009	2	0	2	1	2	2	7.8	57	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	4-20-2009	2			5
490233D	Sivakami R	36	2	2009	7-3-2009	0	0	1	3	2	3	29.5	58	1	1	2	1	1	2	2	2	7,9)(p11-	3	3	1	1	5	7-12-2009	1	3-16-2011	4-6-2011	1
515816D	Sanjeev Khare	36	1	2009	8-5-2009	0	0	2	1	2	2	5.4	76	1	1	2	1	2	2	2	2	46,XY[4]	5		1	1	5	8-17-2009	2			5
449067D	Ashok Gnanaraj	37	1	2009	4-25-2009	2	6	1	3	2	2	37.2	87	1	1	2	1	1	2	2	2	q34;q11.2)der	3	3	1	1	5	5-5-2009	2			5
563659D	Sumathi S	38	2	2009	10-17-2009	0	7	2	1	2	3	26.4	98	1	1	2	1	1	2	2	2	q34;q11.2)(17	3	3	1	1	5	11-9-2009	2		2-10-2010	2
426027D	Indira P R	39	2	2009	3-18-2009	20	10	2	1	2	3	7.7	96	1	1	2	1	2	2	2	2	46,XX[19]	5		1	1	5	3-31-2009	2			5
488494D	Dandapani A	39	1	2009	6-26-2009	2	3	2	1	2	2	116.9	98	1	1	2	1	1	2	2	2	+2,+4,+6,dic(	3	3	1	1	5	7-10-2009	1	10-19-2009	11-21-2009	1
450921D	Amar Saduka	40	1	2009	4-28-2009	3	3	2	1	2	2	3.7	11	1	1	2	1	2	2	2	2	46,XY[20]	5		1	1	5	5-6-2009	2			5
518233D	Vijaya Rani S.	40	2	2009	8-17-2009	3	6	2	1	2	3	147.1	75	1	1	2	1	1	2	2	2	NO	4	3	1	1	5	8-21-2009	1	1-12-2012	2-12-2012	1
560758D	Jai Sankar M	42	1	2009	1-16-2009	2	5	2	1	2	2	0.9	35	1	1	2	1	1	2	2	2	q32;q13.3)[20	5	3	1	1	5	1-24-2009	1	7-17-2012		5
555859D	Kandhaswamy C.	42	1	2009	10-6-2009	7	0	2	1	2	2	78	93	1	3	2	2	2	2	2	2	Not Done	4		1	1	5	10-14-2009	2		11-14-2009	2
577386D	Ranganathan D G	42	1	2009	12-15-2009	1	5	2	1	2	2	2.9	81	1	1	2	1	2	2	2	2	Y,-2,-3,+5,-	3		1	1	5	12-22-2009	1	8-25-2010	10-24-2010	1
536888D	Krishnammal. P	45	2	2009	9-9-2009	2	2	2	1	2	3	2	10	1	1	2	1	2	2	2	2	46,XX[20]	5		1	1	5	9-18-2009	1	9-22-2012	1-17-2013	1
435457D	Arokiasamy M.	46	1	2009	4-2-2009	4	0	2	1	2	2	1	69	1	1	2	1	2	2	2	2	2)(p11.2;p11.	1		1	1	5	4-24-2009	2			5
550882D	Santosh Rai	46	1	2009	9-30-2009	2	0	2	1	2	2	89.4	83	1	1	2	1	1	2	2	2	7,der(9)(t(9;22)	3	3	1	1	5	10-12-2009	1	4-15-2012	9-9-2012	1
599045D	Pandian P	47	1	2009	12-9-2009	0	0	2	1	2	2	6.9	95	1	1	2	1	1	2	2	2	7,t(9;22)(q34;	3	3	1	1	5	12-17-2009	2		7-8-2010	2
436063D	Rana Bahadur Tara	48	1	2009	4-3-2009	4	0	2	1	2	2	2	39	1	1	2	1	1	2	2	2	46,XY[20]	5	3	1	1	5	4-16-2009	2			5
382149D	Somasundaram P	50	1	2009	1-2-2009	0	0	2	1	2	2	9.2	96	1	1	2	1	2	2	2	2	46,XY[20]	5		1	1	5	1-5-2009	2			5
535496D	Dori Chamka Divakar	51	1	2009	9-14-2009	1	0	2	1	2	2	4.2	62	1	1	2	1	2	2	2	2	46,XY[7]	5		1	1	5	9-25-2009	1	6-20-2011	7-20-2011	2

458219D	Subramanian B	56	2	2009	5-9-2009	2	0	1	3	2	3	3.6	86	1	2	2	1	2	2	1	2	46,XY[20]	5	3	1	1	5	5-20-2009	2			5
465280D	Balakrishnan	58	1	2009	5-23-2009	3	2	2	1	2	2	61	92	1	3	2	2	2	2	2	2	46,XY,t(1;6)(q12;q13)46,X	5	4	1	1	5	5-30-2009	2		8-3-2009	1
390485D	Kadeeja	60	2	2009	1-30-2009	0	3	2	1	2	3	62.4	80	1	1	2	1	2	2	2	2	46,XX,inv(1)(p11q12)[20]	5	4	1	1	5	1-30-2009	1	5-21-2009	7-1-2009	1
543179D	Palanisamy K	60	1	2009	9-22-2009	0	0	1	3	2	2	1.6	98	1	1	2	1	1	2	2	2	Not Done	4	3	1	1	5	9-29-2009	2			5
471752D	Rajammal T	63	2	2009	6-4-2009	0	0	2	1	2	3	6.8	0	2	1	2	2	2	2	2	2	Not done	4	4	1	1	5	6-19-2009	2			5
267369D	Mrinmoy Biswas	15	1	2008	7-3-2008	3	0	2	1	2	2	0.7	74	1	1	2	1	2	2	2	2	46,XY,del(1;9)(p11;p11)[5]/46,XY	5	1	1	1	5	7-4-2008	2			5
274095D	Annitha Esther Pal	15	2	2008	7-18-2008	0	0	2	1	2	3	12.26	93	1	1	2	1	2	2	2	1	46,XX,del(1)(q21;q23)t(1;19)(q23;p1	2	1	1	1	5	7-23-2008	1	12-30-2008	5-6-2009	1
214733D	Vasanth	16	1	2008	4-3-2008	5	0	2	1	2	2	0.4	64	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11.2)[4]/	3	3	1	1	5	4-14-2008	2			5
232562D	Katam Ragaveni	16	2	2008	5-14-2008	3	2	2	1	2	3	16.1	24	1	3	2	1	2	2	2	2	46,XX[12]	5	1	1	1	5	5-17-2008	2			5
261588D	Fujit Mahato	16	1	2008	6-20-2008	4	2	2	1	2	2	58.1	92	1	1	2	1	2	2	2	1	46,XY,del(1)(q21;q23)t(1;19)(q23;p1	2	4	1	1	5	6-30-2008	1	9-11-2009	1-22-2010	1
272385D	Tajender Singh	16	1	2008	9-18-2008	5	9	2	1	2	2	3.9	98	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	9-18-2008	1	9-1-2009	11-13-2009	1
278912D	Shuchintha S	16	1	2008	7-22-2008	10	0	2	1	2	2	4.3	17	1	1	2	1	2	2	2	2	46,XY[19]	5	1	1	1	5	8-9-2008	2			5
302412D	Mohammed Irshad	17	1	2008	8-28-2008	2	7	1	3	2	2	22.4	90	1	1	2	1	2	2	2	2	46,XX,t(4;11)(q21;q23),del(6)(q21q24	3	1	1	1	5	8-29-2008	1	1-30-2010	3-19-2010	1
308228D	Nirmal Kumar Raj	17	1	2008	9-8-2008	3	3	2	1	2	2	42.7	94	1	1	2	1	2	2	2	2	46,XY,del(16)(p11)	5	1	1	1	5	9-8-2008	1	9-21-2009	2-8-2010	1
346862D	Indumathi	17	2	2008	11-10-2008	0	0	2	1	2	3	1	75	1	1	2	1	2	2	2	2	45~56,X,-Y,+4,+6,+9,+10,	1	1	1	1	5	11-19-2008	2			5
377727D	Chidananda	17	1	2008	12-23-2008	0	0	1	3	2	2	2.4	70	1	1	2	2	2	2	2	2	46,XY,del(1)(p11)(7)(q10)[20]	5	1	1	1	5	12-26-2008	2			5
205227D	Arun Kumar R S	18	1	2008	5-10-2008	4	4	2	1	2	2	8.6	28	1	1	2	1	2	2	2	2	47~59,XY,+X,+5,+8,del(12)(	1	1	1	1	5	5-10-2008	2			5
284192D	Hari Shankar Prusty B	18	1	2008	8-4-2008	2	0	2	1	2	2	1	70	1	3	2	1	2	2	2	2	81~84,XXYY,-Y,-1,-2,-4,-12,	5	1	1	1	5	8-26-2008	2			5
306749D	Prasanjit Paul	18	1	2008	9-4-2008	4	0	2	1	2	2	4.1	27	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	9-8-2008	2			5
326271D	Rajalakshmi	18	2	2008	10-3-2008	0	0	2	1	2	3	3.8	90	1	1	2	1	2	2	2	2	46,XX,del(3)(q10)(q26)[3]/46,X	5	1	1	1	5	10-3-2008	2			5
378880D	Nishanth K	18	1	2008	12-30-2008	0	0	2	1	2	2	0.9	90	1	1	2	2	2	2	2	2	46,XY[7]	5	1	1	1	5	1-1-2009	2			5
166328D	Gnanasekar K	19	1	2008	1-14-2008	6	7	2	1	2	2	14.5	88	1	1	2	1	2	2	2	2	46,XY,t(2;6)(p10;q21)[2]/46,XY,+2	3	3	1	1	5	1-22-2008	2		4-3-2008	1
245372D	Samuel Joseph Pangani	19	1	2008	5-24-2008	0	0	2	1	2	2	162.7	98	1	1	2	1	2	2	2	2	47,XY,+21[4]/46,XY[7]	1	4	1	1	5	7-1-2008	2			5
220812D	Naveen B S	19	1	2008	9-24-2008	0	0	2	1	2	2	1.2	94	1	1	2	1	2	2	2	2	46,XY[18]	5	1	1	1	5	10-1-2008	2			5
285537D	Anjan Chatterjee	20	1	2008	8-2-2008	0	0	2	1	2	2	1.5	83	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	8-6-2008	2			5
326034D	Jitendra Kumar	20	1	2008	10-1-2008	2	9	2	1	1	2	730	56	1	3	2	2	2	2	2	2	46,XY[5]	5	5	1	1	5	10-1-2008	2			5
209215D	Lenka Gangadhara Naidu	21	1	2008	3-26-2008	0	0	2	1	2	2	7	93	1	1	2	1	1	2	2	2	59~78,XXY,+X,-Y,-	3	3	1	1	5	3-29-2008	2		5-18-2008	1
257881D	Dinesh Kumar	22	1	2008	6-14-2008	0	0	1	3	2	2	4	96	1	3	2	2	2	2	2	2	46,XY[20]	5	1	1	1	5	6-28-2008	2			5
186028D	Kamaladevika	23	2	2008	2-15-2008	5	3	1	3	2	3	233.8	90	1	1	2	1	2	2	2	2	46,XX[20]	5	5	1	1	5	3-7-2008	1	4-14-2009	4-22-2009	1
227585D	Rakesh S	23	1	2008	4-28-2008	3	0	2	1	2	2	39	93	1	3	2	1	2	2	2	2	45,XY,-5,-7,del(7)(p15)	3	3	1	1	5	5-4-2008	2			5
203262D	Parimala	24	2	2008	3-20-2008	4	5	2	1	2	3	1.2	95.5	2	5	2	1	2	2	2	2	46,XX[17]	5	1	1	1	5	4-1-2008	1	12-27-2010	3-9-2011	1
321223D	Shaik Asma Nasreen	24	2	2008	9-24-2008	3	2	2	1	2	3	104.7	98	1	1	2	1	2	2	2	1	46,XX[15]	5	4	1	1	5	9-29-2008	1	9-16-2009	12-1-2009	1
375618B	Arunachalam K	24	1	2008	7-31-2008	0	0	2	1	2	2	20.2	70	1	1	2	1	2	2	2	2	46,XY[17]	5	1	1	1	5	8-2-2008	2			5
313545D	Rajesh Yadav	25	1	2008	9-16-2008	8	10	1	3	1	2	27	26	1	3	2	2	2	2	2	2	Not Done	4	1	1	1	5	9-30-2008	1	5-29-2013	6-29-2013	1
343800D	Shijo Varghese	26	1	2008	11-3-2008	3	0	2	1	2	2	10.2	70	1	1	2	1	2	2	2	2	46,XY[18]	5	1	1	1	5	11-3-2008	2			5
376995D	Mohammd Siraz uddin	26	1	2008	12-22-2008	0	0	2	1	2	2	2	0	1	3	2	2	2	2	2	2	46,XY,t(10;14)(q24;q11)[13]/	5	1	1	1	5	12-26-2008	2			5
198584D	Nagana Gowda T	28	1	2008	3-6-2008	6	8	2	1	2	2	26	89	1	1	2	1	2	2	2	2	43~46,XY,del(6)(q16q24),t(9	3	1	1	1	5	3-7-2008	2			5
361607D	Vinodhini M	29	2	2008	8-27-2008	4	3	2	1	2	3	96	93	1	3	2	2	2	2	2	2	46,XX,del(3)(p22),inv(14)(q	5	1	1	1	5	8-28-2008	2			5
327318D	Siva Kumar K.	31	1	2008	10-3-2008	0	0	1	3	2	2	3.9	40	1	1	2	1	2	2	2	2	46,XY,del(9)(q21q22)[4]/47,XY	5	1	1	1	5	10-12-2008	1	2-17-2009	2-22-2010	1
360946D	Rajina Begam	31	2	2008	12-6-2008	0	0	2	1	2	3	17.4	38	1	1	2	4	1	2	2	2	46,XX,t(9;22)(q34;q11.2)[1c	3	3	1	1	5	12-13-2008	1	3-2-2010	4-5-2010	1
201373D	Patricia Phillips	32	2	2008	3-12-2008	3	0	2	1	2	3	1.7	76	1	1	2	1	1	2	2	2	46,XX,t(9;22)(q34;q11.2)[1	3	3	1	1	5	3-14-2008	2			5
342895D	Soosan Mathew	32	2	2008	10-27-2008	3	3	2	1	2	3	318.2	82	1	3	2	1	2	2	2	2	46,XX[20]	5	5	1	1	5	11-4-2008	2			5
204641D	Amsaveni	34	2	2008	3-16-2008	1	3	2	1	2	3	1.9	10	1	1	2	1	2	2	2	2	45~51,XX,+X,+4,+	1	1	1	1	5	3-29-2008	2			5
228482D	Jothi K	35	2	2008	4-29-2008	0	0	2	1	2	3	0.9	0	1	1	2	1	1	2	2	2	47,XX,del(9)(p13),+mar[cp5]/	5	3	1	1	5	5-9-2008	2			5
208907D	Ramla Sweetlin	35	2	2008	9-6-2008	1	3	2	1	2	3	6.3	95.2	1	2	2	1	2	2	2	2	46,XX[20]	5	5	1	1	5	9-9-2008	1	1-20-2009	3-2-2009	1
197774D	Sunandini Levan	36	2	2008	3-9-2008	0	2	2	1	2	3	2.5	2	1	1	2	1	2	2	2	2	46,XX,t(1;19)(q23;p13.3),d	3	4	1	1	5	3-9-2008	2			5
204294D	Ananthakumar K	36	1	2008	3-17-2008	0	0	2	1	2	2	0.9	74	1	1	2	1	2	2	2	2	46,XY,del(17)(p11.2)[3]/46,	5	1	1	1	5	3-25-2008	1	3-23-2010	5-5-2010	1
311839D	Rajesh Srivastav	40	1	2008	9-10-2008	4	0	1	3	2	2	3.9	98	1	1	2	1	2	2	2	2	Not to Process	4	4	1	1	5	9-15-2008	1	9-4-2009	10-9-2009	1
193297D	Santhi M	41	2	2008	3-5-2008	1	0	1	3	2	2	16.1	65	1	2	2	1	2	2	2	2	46,XX,t(9;22)(q13;q34)t(12;19)(p13)[8]/46,X	5	4	1	1	5	3-7-2008	2			5
196355D	George	41	1	2008	3-8-2008	0	0	2	1	2	2	4	40	1	3	2	1	2	2	2	2	46,XX,t(1;19)(q21;q13)THE 18	5	4	1	1	5	5-5-2008	1	3-28-2012	6-9-2012	1
270584D	Narendran N	44	1	2008	7-8-2008	2	1	2	1	2	2	4.3	2	1	1	2	1	2	2	2	2	46,XY[20]	5	4	1	1	5	7-12-2008	1	3-4-2009	4-30-2009	1

915096C	Arulmani	47	1	2008	8-22-2008	4	2	2	1	2	2	12.5	90	1	1	2	1	2	2	2	2	47,XY,+4,(7;9)46,XY[12]	1		1		5	8-24-2008	2				5
346811D	Perumal P	49	1	2008	11-7-2008	6	7	2	1	2	2	8.3	15	1	1	2	1	2	2	2	2	46,XY[20]	5		1		5	11-19-2008	1	2-24-2009	4-11-2009		1
348373D	Gopalakrishnan	53	1	2008	11-6-2008	0	0	2	1	2	2	0.4	0	1	1	2	1	2	2	2	2	46,XY[16]	5		1		5	11-7-2008	2				5
354131D	Govindaswamy R V	55	1	2008	11-12-2008	0	0	2	1	2	2	2.3	94	1	1	2	1	2	2	2	2	TWO POOR QULAITY	4		1		5	11-14-2008	2				5
233250D	Ramamoorthy D	61	1	2008	5-8-2008	0	0	2	1	2	2	11	31	1	1	2	1	2	2	2	2	46,XY,del(p(1)(q21q32),add(	3	3	1		5	5-30-2008	2		7-31-2008		1
337931D	Wasnew Fisehiveetal Abraham	63	1	2008	10-28-2008	6	3	2	1	2	2	2.7	83	1	1	2	1	2	2	2	2	46,XY[17]	5		1		5	12-2-2008	2				5
964206D	Kullammal M	65	2	2008	12-1-2008	4	0	2	1	2	2	1.9	87	1	2	2	2	2	2	2	2	46~46,XX,-10,-16,-	3		1		5	12-4-2008	2				5
035054D	Aravind E	15	1	2007	5-30-2007	6	10	2	1	2	2	289	99	1	1	2	1	2	2	2	1	46,XY,der(19)t(1;19)(q23;p1	2		1		5	7-10-2007	2				5
158727D	Renita Florence A	15	2	2007	12-22-2007	0	3	2	1	2	3	16.7	80	1	1	2	2	2	2	2	2	46,XX[20]	5		1		5	12-30-2007	2				5
068580D	Nelson Babu M	16	1	2007	7-23-2007	0	4	2	1	2	2	427	90	1	1	2	1	2	2	2	2	46,XY,del(3)(q29)?,add(3)(q29)?i	5	3	1		5	7-25-2007	1	12-13-2007	1-13-2008		1
966475C	Abdul Raheim M	16	1	2007	1-23-2007	0	0	2	1	2	2	366.3	90	1	3	2	2	2	2	2	2	46,XY,del(9)(q21q27)[3]	5		1		5	1-23-2007	1	6-25-2007	7-25-2007		1
969755C	Sheetal Basnet	16	2	2007	1-29-2007	0	0	2	1	1	3	38	59	1	3	2	2	2	2	2	2	46,XX[20]	5	1	1		5	2-6-2007	2				5
014343D	Phaneendra Kumar G	17	1	2007	4-21-2007	2	3	2	1	2	2	1.8	8	1	1	2	1	2	2	2	2	46~46,XY,del(9)(p21),-12,-	3	1	1		5	4-28-2007	2				5
045077D	Allwyan Franklin	17	1	2007	6-13-2007	8	14	1	3	2	2	254.2	96	1	1	2	1	2	2	2	2	46,XY[20]	5		1		5	6-20-2007	2				5
061454D	Bandhu Prasad Rao S	17	1	2007	7-12-2007	0	0	2	1	2	2	24.5	82	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1		5	7-12-2007	2				5
048119D	Shanmugapriya A.	18	2	2007	6-20-2007	2	2	1	3	2	3	27.3	83	1	1	2	1	2	2	2	2	47,XX,+9,(7;9)45~47,XX,+11,-	1	1	1		5	6-30-2007	2				5
960236C	Roshan C P	18	1	2007	1-17-2007	0	0	2	1	2	2	1.3	90	1	1	2	1	2	2	2	2	45,XY,del(3)(12)[p13;p13][4]	1	1	1		5	1-17-2007	2				5
972293C	Dinesh A	18	1	2007	2-2-2007	0	0	2	1	2	2	1.2	91	1	1	2	1	2	2	2	2	46,XY,del(9)?,add(9)(p24)?[5]	5	1	1		5	2-2-2007	2				5
085830D	Keerthana R	19	2	2007	8-25-2007	5	3	1	3	2	3	4.9	86	1	2	2	1	2	2	2	2	46~47,XX,+7,+8,-X,-X,+1,+2,-	3	1	1		5	8-27-2007	2				5
103167D	Meganathan	19	1	2007	9-21-2007	0	0	2	1	2	2	51.9	67	1	1	2	1	2	2	2	2	46,XY,+1,der(1;4)+4,+7,der(4;9)(q10)-,10,-	5	1	1		5	9-22-2007	1	2-22-2008	8-30-2008		1
124517D	Paneerselvam B	19	1	2007	10-23-2007	5	3	1	3	2	2	319	67	1	3	2	2	2	2	2	2	46,XY,t(11;14)(p13;q11)[20]	5	1	1		5	10-31-2007	2				5
015170D	Bharat D Dambal	20	1	2007	5-7-2007	2	0	2	1	2	2	0.5	0	2	5	2	1	2	2	2	2	UNCT, ONE POOR	4		1		5	5-17-2007	2				5
117312D	Aditya K.V.N	20	1	2007	10-10-2007	0	8	2	1	2	2	19.3	94	1	1	2	1	2	2	2	2	92~93,XY,der(7)?dic(7;9)(p	3	3	1		5	10-17-2007	1	7-9-2010	8-5-2010		1
133521D	Dipjyoti Baruah	20	1	2007	11-7-2007	0	0	2	1	2	2	4.8	0	1	1	2	1	2	2	2	2	46,X,r(Y)(q10)[7]/ 46,X,Y[17]	5	1	1		5	11-18-2007	2				5
987692C	Sivasakthivel R	20	1	2007	3-5-2007	0	0	2	1	2	2	229.2	56	1	3	2	1	2	2	2	2	46~49,XY,del(1)(q32.2)[8]/46,XY,del(8)(q10) or	1	3	1		5	3-5-2007	1	2-1-2008	3-22-2008		1
130460D	Kamal Jit Singh	21	1	2007	11-5-2007	5	7	2	1	2	2	6.7	55	1	1	2	1	1	2	2	2	46,XY,-X,del(12)(p13)[	3	3	1		5	11-7-2007	2				5
957267C	Stalin	21	1	2007	1-8-2007	0	0	1	3	2	2	2.5	55	1	1	2	1	2	2	2	2	X,del(12)(p13)[	3	1	1		5	1-8-2007	2				5
970690C	Ranjan Kumar Sahu	21	1	2007	1-30-2007	2	2	2	1	2	2	3.9	61	1	1	2	1	2	2	2	2	46,XY,+8,dic(9;12)(p13;p11	1	1	1		5	1-30-2007	2				5
990088C	Kinlay Rabgay	21	1	2007	3-13-2007	0	0	2	1	2	2	17.8	90	1	1	2	1	2	2	2	2	45,X,-20[3]/46,XY[1	5	1	1		5	3-13-2007	2				5
982167C	Bharathi P	22	2	2007	2-26-2007	0	0	2	1	2	3	9.3	70	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1		5	3-5-2007	2		4-13-2007		2
009522D	Swadhini V.	24	2	2007	4-12-2007	0	2	2	1	2	3	9.1	83	1	1	2	1	2	2	2	2	46,XX,del(12)(p13)[2]/46,X	5	1	1		5	4-13-2007	2				5
025203D	Johanan James	24	1	2007	5-12-2007	5	5	2	1	1	2	202	70	1	3	2	2	2	2	2	2	47,XY,+15,9)/46,XY[7]	1		1		5	5-19-2007	2				5
128667D	Selvarasa Deni Jude	24	1	2007	10-30-2007	3	0	2	1	2	2	7	0	1	3	2	1	2	2	2	2	46,XY[19]	5	1	1		5	11-6-2007	1	3-13-2009	4-16-2009		1
975364C	Baskar C	24	1	2007	2-9-2007	0	0	2	1	2	2	25.8	80	1	1	2	1	1	2	2	2	46,XY[20]	5	3	1		5	2-9-2007	2				5
013166D	Siva Subramani S	25	1	2007	4-23-2007	0	0	2	1	2	2	2.4	8	1	1	2	1	1	2	2	2	46,XX,t(Z;Z)(q34;q11)[7]/4	3	3	1		5	5-2-2007	2				5
040089Q	Rajendra Prasad A.	26	1	2007	6-4-2007	3	1	2	1	2	2	5.2	49	1	1	2	1	2	2	2	2	46,XY[8]	5	1	1		5	7-3-2007	2				5
073804D	Dr Ashok Kumar R	26	1	2007	7-30-2007	0	5	2	1	2	2	44.4	87	1	1	2	1	2	2	2	2	46,XY[30]	5		1		5	8-8-2007	1	9-9-2011	1-27-2012		1
124323D	Subhalaxmi Rath	26	2	2007	10-22-2007	0	0	2	1	2	3	6.4	36	1	1	2	1	2	2	2	2	46,XX[19]	5		1		5	10-29-2007	2				5
118257D	Indumathi	27	2	2007	10-11-2007	0	0	2	1	2	3	3	84	1	3	2	2	2	2	2	2	46,XX,t(10;11)(p13;q21)[10]	3	1	1		5	10-20-2007	2				5
981651C	Rajat Mondal	27	1	2007	2-23-2007	6	4	2	1	2	2	4	37	1	1	2	2	2	2	2	2	46,X,-Y,+mar[10]/46	5	1	1		5	5-13-2007	2				5
133764D	Kunal Divyakumar Randeria	28	1	2007	11-12-2007	0	0	2	1	2	2	2.9	10.8	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1		5	11-12-2007	2				5
074508D	Akila C.	29	2	2007	8-19-2007	0	3	2	1	2	3	7.5	0	1	1	2	1	2	2	2	2	46,XX[20]	5	1	1		5	8-19-2007	2				5
092363D	Malar	29	2	2007	9-3-2007	11	4	2	1	2	3	37.5	88	1	1	2	1	2	2	2	1	46,XX,t(1;9)(q23;p13.3)[10	2	1	1		5	9-10-2007	1	3-14-2008	4-14-2008		1
143814D	Gayathri R.	29	2	2007	11-23-2007	0	0	2	1	2	3	351.4	95	1	2	2	1	2	2	1	2	46,XX,t(1;9)(q21;q23)[18]/	3		1		5	11-23-2007	2				5
031988D	Desikachari M J	30	1	2007	5-23-2007	6	3	2	1	2	2	309	95	1	3	2	2	2	2	2	2	47,XY,+8,-14,+22[3]/47,-	1	1	1		5	5-23-2007	2				5
157226D	Sajitha Sivaprakasan	30	2	2007	12-21-2007	0	0	1	3	2	3	21	40	1	3	2	1	2	2	2	2	47,XX,+4,r(9;22,XXXX[3]/46,	1	1	1		5	12-21-2007	1	4-18-2012	5-12-2013		1
118984D	Sathiya R	33	2	2007	10-15-2007	0	0	2	1	2	3	2	82	1	2	2	2	2	2	2	2	46,XX,t(1;9)(q10;q11)[15]/45,idem	5		1		5	10-15-2007	1	3-25-2008	4-25-2008		1
004197D	Shanthi S.	37	2	2007	4-3-2007	0	0	2	1	2	3	240.4	94	1	1	2	1	1	2	2	2	45~46,XX,-9,del(9)(q21),-	3	3	1		5	4-6-2007	1	10-27-2009	8-30-2010		1
055631D	Suchan Mishra	37	1	2007	6-30-2007	2	0	2	1	2	2	1.9	74	1	3	2	2	2	2	2	2	91~93,X,-Y,+del(1)(p32)+2~4[3],X,-	3		1		5	7-13-2007	2				5
125521D	Ashifuzzaman	39	1	2007	10-24-2007	6	4	2	1	2	2	7.2	85	1	1	2	1	2	2	2	2	42~45,X,-16,+19,-	3		1		5	11-2-2007	1	1-25-2010	5-29-2010		1

979394C	Anup Saha	39	1	2007	3-22-2007	4	2	2	1	2	2	5.1	48	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	3-22-2007	1	1-23-2010	2-25-2010	1
151657D	Seethalakshmi R	44	2	2007	8-12-2007	0	0	2	1	2	2	12.5	30	1	1	2	2	2	2	2	2	Not Done	4	5	1	1	5	12-10-2007	1	9-22-2009	6-25-2010	1
063931D	Saju Joseph	45	1	2007	7-14-2007	0	0	2	1	2	2	10.1	0	2	5	2	1	2	2	2	2	46,XY[15]	5	5	1	1	5	7-14-2007	2			5
970612C	Chitra Vasudevan	48	2	2007	1-29-2007	3	0	2	1	2	3	10.4	25	1	1	2	1	2	2	2	2	45,XX,-20[18]	5	5	1	1	5	1-29-2007	1	7-25-2008		5
020641D	Kamal Kishore Shaw	52	1	2007	5-4-2007	3	0	2	1	1	2	2	0	1	3	2	2	2	2	2	2	Not Done	4	5	1	1	5	5-13-2007	2			5
074927D	Debebrata Misra	54	1	2007	8-2-2007	0	0	2	1	2	2	0.8	0	1	1	2	1	2	2	2	2	46,XY[3]	5	5	1	1	5	8-10-2007	2		9-8-2007	2
994737C	Elizabeth Sr.	56	2	2007	3-15-2007	0	0	2	1	2	3	3.4	27	1	1	2	1	1	2	2	2	46,XX,del(4)(q12)[4],9	3	3	1	1	5	3-19-2007	2			5
933525D	Vaseekaran G.	63	1	2007	5-24-2007	0	0	2	1	2	2	6.5	91	1	1	2	1	1	2	2	2	46,XY,der(9)t(9;22)(q34;q11	3	3	1	1	5	5-25-2007	2			5
042389D	Kalmappa Nindodappa Patil	67	1	2007	6-14-2007	4	0	2	1	2	2	4.8	15	1	1	2	1	2	2	2	2	46,XY[20]	5	5	1	1	5	6-21-2007	1	10-1-2007	12-24-2007	2
753137C	Md. Nasiruddin Khan	15	1	2006	1-4-2006	4	0	2	1	2	2	1.9	99	1	1	2	1	2	2	2	2	46, XY[1]	5	1	1	1	5	1-5-2006	1	6-26-2007	7-26-2007	1
781435C	Praful Dev K	15	1	2006	2-27-2006	2	1	2	1	2	2	57	98	1	1	2	1	2	2	2	2	46, XY,-3, -4, -5, -7, -9,	5	1	1	1	5	3-1-2006	1	6-29-2010	6-21-2011	2
831055C	Riju Atta	15	1	2006	5-31-2006	3	2	2	1	2	2	246.5	89	1	1	2	1	2	2	2	2	46,XY,del(4)(?q32) [10]	5	1	1	1	5	6-30-2006	2			5
917157C	Vineeth E K	15	1	2006	10-25-2006	2	2	2	1	2	2	1.2	90	1	1	2	1	2	2	2	2	46, XY, del(6)(q21q24	5	1	1	1	5	10-25-2006	2			5
947234C	Siva Kumar	15	1	2006	12-16-2006	0	0	2	1	2	2	242.3	98	1	3	2	2	2	2	2	2	46,XY[10]	5	5	1	1	5	12-16-2006	2			5
774434C	Thasleena V.K.	16	2	2006	2-14-2006	4	2	2	1	2	3	430.7	95	1	3	2	1	2	2	2	2	46,XX,del(6)(q21;q25)[2]/46,	5	5	1	1	5	2-18-2006	2			5
853347C	Femi Francis	16	2	2006	7-10-2006	0	0	2	1	2	3	8.1	27	1	1	2	1	2	2	2	2	46,X,i(X)[8/10] [11] /45,X,-X,	5	1	1	1	5	7-10-2006	2			5
757225C	Nagarjuna B.	17	1	2006	1-7-2006	0	0	2	1	2	2	2.7	2	1	1	2	1	2	2	2	2	UNLY TWO METAPHASE	4	1	1	1	5	1-20-2006	2			5
828095C	Venkatesan	17	1	2006	5-29-2006	3	3	2	1	2	2	86.3	63	1	3	2	1	2	2	2	2	42-45,XY,-18,-21,-22 [cp 5]	3	1	1	1	5	6-3-2006	2		7-30-2006	1
849133C	Abu Backer Siddique	17	1	2006	7-1-2006	5	3	2	1	2	2	3.3	20	1	1	2	1	2	2	2	2	46,XY,t(9)(q10;) [16]	5	1	1	1	5	7-1-2006	1	1-16-2007	7-1-2007	1
876067C	Surya Chanakya K	17	1	2006	8-15-2006	5	2	2	1	2	2	145.7	91	1	1	2	1	2	2	2	2	Not done	4	3	1	1	5	8-17-2006	2		10-8-2006	1
881329C	Siva Kumar K	17	1	2006	8-25-2006	7	0	2	1	2	2	2.5	94	1	1	2	1	2	2	2	2	45, XY, dic(9;12)(p11.2;q13),	1	1	1	1	5	8-25-2006	2			5
758796C	Shake Mohiuddin	18	1	2006	2-6-2006	1	4	2	1	2	2	31	62	1	1	2	1	2	2	2	2	+21[4]/46,	1	1	1	1	5	2-7-2006	2			5
784274C	Shayan Mukherjee	18	1	2006	3-2-2006	4	7	2	1	2	2	114	38	1	3	2	2	2	2	2	2	87-91,XXYY,-2,-4,-4,-5,-6,-	5	1	1	1	5	3-3-2006	2			5
803304C	Keka Ghosh	18	2	2006	4-11-2006	0	0	2	1	2	3	4.2	29	1	1	2	1	2	2	2	2	46, XX[19]	5	1	1	1	5	4-24-2006	1	12-5-2012	1-5-2013	1
816877C	Arun Kumar N	18	1	2006	5-4-2006	2	0	2	1	2	2	5.5	66	1	1	2	1	2	2	2	2	49, XY, +X, +7, +8[2]/49,	1	1	1	1	5	5-8-2006	2			5
828283C	Rohit Chakravarty	18	1	2006	6-3-2006	0	0	2	1	2	2	65.7	90	1	1	2	1	2	2	2	2	48,XY,+4,+21 [2] /46,XY [2]	1	5	1	1	5	6-4-2006	2		7-27-2006	1
758970C	Agustin R	19	1	2006	1-18-2006	0	3	2	1	2	2	3.5	18	1	1	2	1	2	2	2	2	SC,-Y, +6,+7,+8,+11,	1	1	1	1	5	1-19-2006	2			5
811390C	Kashyap	20	1	2006	4-24-2006	0	0	2	1	2	2	7.5	47	1	2	2	1	2	2	2	2	46,XY [20]	5	3	1	1	5	4-24-2006	1	1-11-2007	10-10-2007	1
836203C	Deepak Kumar	21	1	2006	2-25-2006	0	0	2	1	2	2	9	1	1	1	2	2	2	2	2	2	46,XY[20]	5	3	1	1	5	6-25-2006	2			5
851921C	Bakkiyaraj P	21	1	2006	7-5-2006	2	3	2	1	2	2	10.5	55	1	1	2	1	2	2	2	2	53-56,XY,+X, +2,+4,+5,+6,+	1	1	1	1	5	7-5-2006	2			5
942535C	Alphy Kurien	21	1	2006	12-6-2006	0	0	2	1	2	2	1.3	0	1	2	2	1	1	2	2	2	46,XY[2]	5	3	1	1	5	12-6-2006	1	7-24-2008	8-24-2008	1
764613C	Prakash	23	1	2006	1-24-2006	5	3	2	1	2	2	11	45	1	1	2	1	2	2	2	2	46,XY [20]	5	1	1	1	5	1-25-2006	2			5
896258C	Babu	23	1	2006	10-5-2006	0	0	2	1	2	2	7.5	26	1	3	2	2	2	2	2	2	46, XY[18]	5	1	1	1	5	10-5-2006	2			5
923898C	Pintu Basak	23	1	2006	11-10-2006	2	2	2	1	2	2	23.5	98	1	2	2	1	2	2	2	2	43-47,XY,del(6)(q21q25),+7	3	1	1	1	5	11-10-2006	2		12-20-2007	1
812132C	Sandhya	24	2	2006	5-1-2006	7	3	2	1	2	3	70.4	88	1	1	2	1	2	2	2	1	46,XX,del(19)t(1;19)(q23;p1	2	1	1	1	5	5-1-2006	1	9-16-2008	2-13-2009	1
903173C	Aruna Laxmi Prasanna	24	2	2006	10-4-2006	0	0	2	1	2	3	1.4	0	1	2	2	1	2	2	2	2	46,XY[9]	5	1	1	1	5	10-4-2006	1	3-8-2010	9-5-2010	1
757247C	John Moses G	25	1	2006	1-7-2006	0	0	2	1	2	2	1.1	18	1	3	2	1	2	2	2	2	46, XY[5]	5	1	1	1	5	1-13-2006	2			5
914715C	Mita Samanta	25	2	2006	10-26-2006	0	0	2	1	2	3	10.5	22	1	3	2	2	2	2	2	2	46, XX, del(6)(q21q24	5	1	1	1	5	10-26-2006	1	12-30-2010	3-24-2011	1
779391C	Abhjit Das	26	1	2006	2-28-2006	3	0	2	1	1	2	102	40	1	3	2	2	2	2	2	2	Not done	4	5	1	1	5	2-28-2006	2			5
839500C	Anu Radha Jaiswal	26	2	2006	6-28-2006	1	3	2	1	2	3	12.4	0	1	3	2	2	2	2	2	2	44-46,XX,-8,-9,-14,+ mar	5	1	1	1	5	6-29-2006	2			5
864620C	Karthik T S	26	1	2006	7-27-2006	4	2	2	1	2	2	184.6	98	1	3	2	1	2	1	2	2	46,XY [20]	5	5	1	1	5	7-27-2006	2		10-3-2006	2
896113C	Raja	27	1	2006	9-20-2006	0	4	2	1	2	2	14.2	85	1	3	2	2	2	2	2	2	46, XY[15]	5	1	1	1	5	9-21-2006	2			5
818873C	Velmurugan P	28	1	2006	7-19-2006	3	2	2	1	2	2	1.2	90	1	3	2	1	2	2	2	2	46,XY[6]	5	1	1	1	5	7-19-2006	2			5
946506C	Doddi Prasad	29	1	2006	12-13-2006	0	0	2	1	2	2	1.8	91	1	2	2	1	2	2	2	2	46,XY[6]	5	1	1	1	5	12-13-2006	1	4-20-2010	1-17-2011	1
865812C	Rajeswari T	30	2	2006	9-29-2006	0	3	2	1	2	3	0.5	0	1	3	2	2	2	2	2	2	46, XX[2]	5	1	1	1	5	9-29-2006	1	1-6-2007	4-10-2007	1
906830C	Nikunj Kishore Benu	30	1	2006	10-9-2006	0	0	2	1	2	2	7.9	32	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11.2)[4]/	3	3	1	1	5	10-9-2006	2		4-1-2007	2
941205C	Durga Devi A	31	2	2006	12-7-2006	6	3	2	1	2	3	246.6	88	1	3	2	2	2	2	2	2	Not done	4	5	1	1	5	12-13-2006	2			5
753536C	Prince	33	1	2006	1-4-2006	3	0	1	3	2	2	20.7	13	1	1	2	1	2	2	2	2	46, XXY, -1, -2, -3, -4, -7, -8,	3	1	1	1	5	1-5-2006	1	3-27-2008	5-18-2006	1
894622C	Karakatty F	34	1	2006	9-16-2006	0	0	2	1	2	2	1.1	23	1	1	2	1	2	2	2	2	46, XY[8]	5	1	1	1	5	9-16-2006	2			5
863074C	Anwar Basha	36	1	2006	7-25-2006	3	0	2	1	2	2	118.7	99	1	1	2	1	2	2	2	2	46, XY[20]	5	3	1	1	5	7-25-2006	2			5

801650C	Suraja K.C.	37	2	2006	4-4-2006	6	14	2	1	2	3	0.5	96	1	1	2	1	2	2	2	2	46, XX[15]	5		1		5	7-4-2006	2		10-5-2006	2
850468C	Prasanna Kumar	37	1	2006	7-12-2006	0	0	2	1	2	2	23.3	99	1	1	2	1	2	2	2	2	47,XY,+X,del(3)(?q13.3)(q21;	4	3	1		5	7-12-2006	1	12-4-2006	1-8-2007	1
810542C	Gopu V	38	1	2006	4-24-2006	3	5	2	1	2	2	86.7	84	1	1	2	1	2	2	2	2	45,XY, - 7,del(8)(p?22	2	3	1		5	4-24-2006	2		9-18-2006	1
936999C	Murugan V	38	1	2006	11-27-2006	0	0	2	1	2	2	10.3	45	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11)[2]	3	3	1		5	11-27-2006	1	12-29-2009	2-5-2010	1
849596C	Karunakaran R	39	1	2006	7-1-2006	0	0	2	1	2	2	2.9	0	1	1	2	1	2	2	2	2	46,XY,del(20)(q12) [2] /	5		1		5	7-1-2006	2		5-4-2007	2
863562C	Shanmugam R	39	1	2006	7-25-2006	2	3	2	1	2	2	155	93	1	1	2	1	2	2	2	2	46,XY[2]	5		1		5	7-25-2006	1	1-5-2007	8-2-2007	1
872499C	Nagarajan M	42	1	2006	8-10-2006	0	0	1	3	2	2	88.7	89	1	1	2	1	2	1	2	2	46,XY [18]	5		1		5	8-10-2006	1	12-24-2007	4-5-2008	1
885472C	Celine Thomas	43	2	2006	9-2-2006	4	3	2	1	2	3	3.3	20	1	2	2	1	2	2	2	2	35-36,X,-X,-3,-4,-5,6,-7,-8,-9,	3		1		5	9-2-2006	1	11-10-2007	10-12-2007	1
909729C	Rajamani N	45	1	2006	10-13-2006	0	2	2	1	2	2	5.2	25	1	1	2	1	1	2	2	2	46, XX [8]	5	3	1		5	10-13-2006	1	4-23-2008	8-22-2008	1
915040C	Kamal kumar sarkar	48	1	2006	10-21-2006	0	0	2	1	2	2	2.5	0	1	2	2	1	1	2	2	2	46, XY, t(9;22)(q34;q1	3	3	1		5	11-2-2006	1	1-29-2008	10-1-2009	1
928260C	Ramasamy	50	1	2006	11-14-2006	6	0	2	1	2	2	3.7	0	1	1	2	1	2	2	2	2	Not done	4		1		5	11-14-2006	1	9-7-2007	8-19-2007	1
889966C	Ramadevi	54	2	2006	9-12-2006	8	8	1	3	2	3	9.9	58	1	1	2	1	2	2	2	2	48, XX, +X, del(3)(q13),	3		1		5	9-12-2006	2		7-5-2007	2
853180C	Nisthar	56	1	2006	7-10-2006	0	0	2	1	2	2	8.6	26	1	1	2	1	2	2	2	2	46,XY[3]	5		1		5	7-10-2006	1	5-12-2007	6-12-2007	1
806051C	Debnarayan Dey	57	1	2006	4-12-2006	2	0	2	1	2	2	1.9	0	1	1	2	1	2	2	2	2	46,XY [12]	5		1		5	5-19-2006	2			5
797179C	Hema Venkiteswaran	58	2	2006	3-25-2006	0	0	2	1	2	3	34.9	76	1	1	2	1	1	2	2	2	46,XX,t(9;22)(q34;q11)[17] /	3	3	1		5	3-29-2006	1	6-12-2007	7-12-2007	1
855542C	Satyanarayana L	59	1	2006	7-12-2006	2	0	2	1	2	2	6.8	35	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11),del(	3	3	1		5	7-13-2006	2			5
788228C	Ramappan A K	67	1	2006	3-11-2006	0	0	2	1	2	2	5.5	20	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11) [5] /	3	3	1		5	3-15-2006	2			5
669912C	Surendar	15	1	2005	8-3-2005	4	2	2	1	2	2	3	12	1	1	2	1	2	2	2	2	46,XY [16]	5	1	1		5	8-4-2005	2			5
691741C	Manash Saha	15	1	2005	9-6-2005	0	0	2	1	2	2	8.9	0	1	1	2	1	2	2	2	2	47,XY,del(11)(q22q31),add(4)	5	1	1		5	9-8-2005	1	11-14-2006	2-19-2007	1
751277C	Rakesh Kumar Pramanik	15	1	2005	12-28-2005	1	0	2	1	2	2	79.5	72	1	1	2	1	2	2	2	2	46, XY[20]	5		1		5	1-5-2006	2			5
634030C	Sargunam	16	1	2005	5-7-2005	5	2	1	3	2	2	9.8	62	1	1	2	1	2	2	2	2	46,XY [20]	5	1	1		5	5-18-2005	1	3-21-2006	6-16-2006	1
665872C	Wangmo	16	2	2005	7-11-2005	2	2	2	1	2	3	92.2	90	1	1	2	1	2	2	2	2	47,XX,+21[10] /	1		1		5	7-14-2005	2			5
697724C	Rekha J	16	2	2005	9-9-2005	4	3	2	1	2	3	17.4	36	1	1	2	1	2	2	2	2	51~52, XX,+3,+4,+10	1	1	1		5	12-9-2005	1	7-23-2007	8-23-2007	2
636916C	Jean Joy	17	2	2005	6-1-2005	2	2	2	1	2	3	19.6	73	1	1	2	1	1	2	2	2	46,XX [17]	5	3	1		5	6-9-2005	2		8-1-2005	1
731411C	Janani P	17	2	2005	11-18-2005	0	0	2	1	2	3	4.1	82	1	1	2	1	2	2	2	1	46, XX, t(1;19)(q23;P1	2	1	1		5	11-19-2005	1	6-8-2006	9-25-2006	1
581461C	Jambay Dorti	19	1	2005	1-12-2005	5	1	2	1	2	2	15.3	0	2	5	2	1	2	2	2	2	46, XY[17]	5	1	1		5	1-20-2005	2			5
590696C	Abdul Rahman.K.T.	19	1	2005	2-2-2005	0	5	2	1	2	2	19.1	65	1	1	2	1	2	2	2	1	Not done	4	1	1		5	2-2-2005	1	9-8-2006	10-17-2006	1
613899C	Mustafa.G.M.	19	1	2005	4-12-2005	4	0	2	1	2	2	9	34	1	1	2	1	2	2	2	2	47,XY, +21[3]/46,	1	1	1		5	4-13-2005	1	5-5-2006	6-19-2006	1
655141C	Gobinda talukdar	19	1	2005	6-21-2005	4	6	2	1	2	2	12.6	56	1	1	2	1	2	1	2	2	46, XY[20]	5		1		5	6-27-2005	2			5
702281C	Saranyan .P	19	1	2005	9-16-2005	0	0	2	1	2	2	1.6	28	1	1	2	1	2	2	2	2	46, XY[2]	5		1		5	9-17-2005	2			5
636039C	Mohan	20	1	2005	5-20-2005	6	7	2	1	2	2	179	60	1	3	2	2	2	2	2	2	Not done	4		1		5	5-21-2005	1	12-11-2006	1-6-2007	2
712558C	Shabeer P.	20	1	2005	10-10-2005	0	0	2	1	2	2	4.7	58	1	1	2	1	2	2	2	2	45~46,XY,del(8)	3	1	1		5	10-25-2005	2			5
669247C	Lipika Maity	21	2	2005	8-11-2005	0	0	2	1	2	3	1.8	0	1	1	2	1	2	2	2	2	46, XX[13]	5	1	1		5	8-17-2005	2			5
725500C	Teena Ramesh	21	2	2005	11-1-2005	2	0	2	1	2	3	39.8	65	1	3	2	2	2	2	2	2	92~93,XXX,-1,-2,del(3)(q25q	3		1		5	11-1-2005	2			5
733721C	Sudipta Banerjee	23	1	2005	11-22-2005	2	15	2	1	2	2	9.4	43	1	1	2	1	2	1	2	2	46,XY [5]	5	1	1		5	11-24-2005	1	5-30-2006	7-2-2006	1
574090C	Raju Chettry	25	1	2005	1-12-2005	0	5	1	3	2	2	115	70	1	3	2	2	2	2	2	2	47, 81,XXYY,+1,+	3		1		5	1-12-2005	2			5
721599C	Nimmy Rajesh	25	2	2005	10-26-2005	3	0	2	1	2	3	5.2	25	1	1	2	1	2	2	2	2	47,XX,add(4)(p16),	3	1	1		5	10-26-2005	2			5
724884C	Vivek Narayan Vallathol	27	1	2005	10-31-2005	5	0	1	3	2	2	45.9	60	1	3	2	2	2	2	2	2	46,XY [5]	5	1	1		5	12-10-2005	2			5
595707C	Manickam.R	30	1	2005	2-14-2005	1	3	2	1	2	2	10	24	1	1	2	1	2	2	2	2	46,XY,del(1)(q31q34),del(9),	5		1		5	2-14-2005	1	6-18-2005	9-19-2005	1
715474C	Md. Janna Ali	32	1	2005	10-31-2005	0	0	2	1	2	2	3.3	0	1	1	2	2	2	2	2	2	46, XY[8]	5	1	1		5	11-14-2005	1	1-25-2011	2-25-2011	1
746671C	Vijayalakshmi B	33	2	2005	12-31-2005	6	2	2	1	2	3	3.3	7	1	1	2	1	1	2	2	2	47, XX, +mar?der(7)[4	5	3	1		5	12-31-2005	2			5
623535C	Sreedeep .E.K.	36	1	2005	4-27-2005	0	0	2	1	2	2	34.3	90	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11) [6] /	3	3	1		5	4-28-2005	1	1-20-2009	6-6-2011	1
633654C	Satyam .C	43	1	2005	5-5-2005	0	0	2	1	2	2	15	55	1	1	2	1	2	2	2	2	51~54,XXY,+2,+4	3		1		5	5-7-2005	2		6-16-2006	1
705351C	Ganesan P.	43	1	2005	9-23-2005	0	6	1	3	2	2	105.8	90	1	2	2	1	2	2	1	2	46,XY, t(4;11)(q21;q2	3	3	1		5	9-24-2005	2		1-7-2006	2
615373C	Venkatesan R.	44	1	2005	4-7-2005	3	0	2	1	2	2	105	92	1	1	2	1	1	2	2	2	47,XY,t(9;22)(q34;q11),	3	3	1		5	4-7-2005	2		7-10-2005	1
707850C	Sundarapandiyan	47	1	2005	9-29-2005	0	0	2	1	2	2	56.4	89	2	5	2	1	1	2	2	2	48~50,XXY,+4,+5	3	3	1		5	9-30-2005	2		11-8-2005	1
672988C	Gowtharman S.P.Dr.	49	1	2005	7-25-2005	0	0	2	1	2	2	0.4	0	1	1	2	1	2	2	2	2	46,XY,t(9;22)(q34;q11)[12] /	5		1		5	7-26-2005	1	6-1-2009	3-14-2012	1
607062C	Ashok Sarkar	51	1	2005	3-14-2005	0	0	2	1	2	2	14.8	58	1	1	2	1	1	2	2	2	46,XY,t(9;22)(q34;q11)[14]/	3	3	1		5	3-16-2005	1	1-25-2008	1-9-2009	2
647045C	Robert T.	53	1	2005	6-6-2005	0	0	2	1	2	2	4.5	0	1	1	2	2	2	2	2	2	Not done	4		1		5	6-14-2005	2			5
659684C	Chandran .A.S	53	1	2005	7-15-2005	5	0	2	1	2	2	44.8	48	1	1	2	1	2	2	2	1	46, XY[20]	5		1		5	7-16-2005	1	12-10-2005	12-18-2005	1

549477C	Chithra Lakshmi	16	2	2004	11-2-2004	0	0	2	1	2	3	96.6	95	1	1	2	2	2	2	2	2	47,XX,del(6)(q15q23),der(19	2		1		5	11-3-2004	1	2-6-2008	9-1-2008	1
408968C	Satish P.	17	1	2004	2-14-2004	2	3	2	1	2	2	30	88	1	3	2	2	2	2	2	2	ONLY 4 POOR	4	1	1	1	5	2-22-2004	2			5
511779C	Daniel.C	17	1	2004	8-25-2004	4	1	2	1	2	2	12.3	71	1	1	2	1	2	1	2	2	Not done	4	1	1	1	5	9-1-2004	2			5
522700C	Mohammed Nainar.S	17	1	2004	9-27-2004	0	0	1	3	2	2	24.7	35	1	3	2	2	2	2	2	2	Not done	4	1	1	1	5	10-22-2004	1	5-17-2005	8-1-2005	1
527884C	Bharani Dharan.D	17	1	2004	9-21-2004	1	4	2	1	2	2	93	89	1	1	2	1	2	2	2	1	46, XY[7]	5		1	1	5	9-21-2004	2			5
556416C	Priyanka Pavithran	18	2	2004	11-16-2004	0	3	2	1	2	3	11.1	69	1	1	2	1	2	2	2	2	THERE ARE NO	4	1	1	1	5	11-16-2004	1	9-1-2010		5
573992C	Chandan Kumar Mantri	18	1	2004	12-27-2004	1	0	2	1	2	2	1.9	0	1	1	2	1	2	2	2	2	THERE ARE NO	4	1	1	1	5	12-29-2004	1	6-5-2006	6-19-2006	1
432347C	Manikandan .K	19	1	2004	2-25-2004	3	3	2	1	2	2	111	90	1	1	2	1	1	2	2	2	46,XY, t(9;22)(q34;q1	3	3	1	1	5	3-5-2004	2			5
432548C	Sakthivel P.	19	1	2004	2-25-2004	0	0	2	1	2	2	38.4	57	1	3	2	2	2	2	2	2	ONLY THREE	4	1	1	1	5	2-26-2004	2			5
420487C	Sauvik Pain	20	1	2004	1-31-2004	0	0	2	1	2	2	118	0	1	1	2	1	1	2	2	2	only a poor quality	4	3	2	1	5	2-4-2004	2			5
526280C	Utpal Barman	21	1	2004	10-15-2004	3	4	2	1	2	2	55	94	1	3	2	1	2	2	2	2	THERE ARE NO	4	1	1	1	5	10-15-2004	1	1-3-2006	2-3-2006	1
541922C	Murali Dhar Jana	21	1	2004	11-5-2004	0	6	2	1	2	2	13	45	1	1	2	1	2	2	2	2	46, XY, -9, add(12)(P11.2	1	1	1	1	5	11-9-2004	2		8-19-2005	2
439544C	Sumathi	22	2	2004	3-18-2004	18	3	2	1	2	3	3.5	33	1	1	2	1	2	2	2	2	ONLY FOUR POOR	4	1	1	1	5	3-24-2004	2			5
360734C	Raji	23	2	2004	2-24-2004	0	0	2	1	2	3	120	89	1	1	2	1	1	2	2	2	46, XX,dup(1)(q1	3	3	1	1	5	2-29-2004	1	4-12-2005	5-12-2006	1
413098C	Balaji.T.N	23	1	2004	1-10-2004	7	8	2	1	2	2	21.1	64	1	1	2	1	2	2	2	2	der(2;7)(XXYY; +4, +6, +8,	1	1	1	1	5	1-12-2004	2			5
441283C	Roby M Mathew	23	1	2004	3-17-2004	4	5	2	1	2	2	26	67	1	1	2	1	1	2	2	2	46, XY, der(2;2),	3	3	1	1	5	3-18-2004	1	12-10-2004	6-10-2005	1
450469C	Naveen.A.H.	24	1	2004	4-7-2004	4	7	2	1	2	2	133	89	1	3	2	2	2	2	2	2	THE METAPHASE	4	3	1	1	5	4-7-2004	1	4-15-2005	5-19-2005	1
565942C	Freeda Mary A.	26	2	2004	11-24-2004	3	0	2	1	2	3	5.6	0	1	1	2	1	2	2	2	2	46,XX[10]	5	1	1	1	5	12-3-2004	1	11-16-2005	12-21-2006	1
509353C	Krishna.T	27	1	2004	8-18-2004	1	5	2	1	2	2	25.6	67	1	1	2	1	2	2	2	2	46,XY [7]	5	1	1	1	5	10-5-2004	2			5
533592C	Mamoiz	28	1	2004	10-1-2004	0	0	2	1	2	2	23.6	0	2	5	2	1	2	2	2	2	There are no metaphase	4	1	1	1	5	10-2-2004	1	8-2-2008	9-5-2008	1
552478C	Sireesh Kumar	28	1	2004	11-10-2004	0	0	1	3	2	2	6	76	1	1	2	1	2	2	2	2	ONLY ONE POOR	4	1	1	1	5	11-10-2004	2			5
418548C	Santhosh.M.P.	30	1	2004	1-23-2004	3	0	2	1	2	2	2.1	83	1	1	2	1	2	2	2	2	46, XY [12]	5	1	1	1	5	1-23-2004	2			5
463216C	Senthil Kumaran.K	32	1	2004	5-10-2004	0	0	2	1	2	2	72.4	37	1	3	2	2	2	2	2	2	46, XY [6]	5	1	1	1	5	5-15-2004	2			5
437257C	Parvata Kumari	34	2	2004	3-11-2004	0	0	2	1	1	3	55	100	1	3	2	2	2	2	2	2	POOR POOR QUALITY	4		1	1	5	3-19-2004	1	9-16-2004	10-16-2004	1
524426C	Muraleedharan.M	35	1	2004	9-21-2004	0	0	2	1	2	2	5.4	0	1	1	2	1	1	2	2	2	54,XXYY,+4, +5, +8, +14,	1	3	1	1	5	9-23-2004	1	8-20-2008	9-22-2008	1
532299C	Rosmi D.	37	2	2004	9-29-2004	0	0	2	1	2	3	4.1	35	1	1	2	1	2	2	2	2	46,XX [3]	5	3	1	1	5	10-1-2004	2			5
476659C	Sajeed A.K.	39	1	2004	1-10-2004	4	14	1	3	2	2	163	90	1	3	2	1	2	2	2	2	46,XY [6]	5	3	1	1	5	6-12-2004	1	5-17-2005	6-15-2005	1
551931C	Ushsrani Sahu	44	2	2004	11-8-2004	0	0	2	1	2	3	4	4	1	1	2	1	1	2	2	2	46,XX,t(9;22)(q34;q11)	3	3	1	1	5	11-10-2004	2		3-24-2005	2
444095C	Sainudheen	51	1	2004	3-30-2004	4	2	2	1	2	2	10.9	23	1	1	2	1	2	2	2	2	46, XY [8]	5	1	1	1	5	3-31-2004	1	4-8-2005	2-14-2005	1
547612C	Sophia Khanam	59	2	2004	11-10-2004	0	0	2	1	2	3	1	0	1	1	2	1	2	2	2	2	Not done	4		1	1	5	11-12-2004	2			5
782218F	Rincy Rajan	22	2	2014	1-13-2014	6	8	2	1	2	3	6.5	89	1	1	1	1	2	2	2	2	44~47,XX,del(1	3		1	1	5	1-16-2014	2			5
754237F	Meena Devi	45	2	2014	2-5-2014	4	8	2	1	2	3	116.1	93	1	1	1	1	2				46,XX,der(9;2	5		1	1	5	2-5-2014	2			5
795577F	Prasad	45	1	2014	2-4-2014	4	3	2	1	2	2	1.4	54	1	1	1	1	2				46,XY[20]	5		1	1	5	2-5-2014	2			5
775764F	Saiful Alam	50	1	2014	1-25-2014	0	0	2	1	2	1	3.1	60	1	3	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	1-31-2014	2			5
750216F	Krishna Samy	58	1	2014	2-6-2014	4	0	2	1	2	2	2.8	34	1	1	1	1	1	3	3	3	46,XY,t(9;12)(	5	3	1	1	5	2-6-2014	2			5
699798F	Devi P	20	2	2013	10-14-2013	0	0	3	7	2	3	49.2	94	1	3	2	2	3	3	3	3	43~45,XX,der	3	1	1	1	5	10-14-2013	2			5
425151F	Prasanthvaidya .S	21	1	2013	3-2-2013	0	1	2	1	2	2	2.8	82	1	1	2	1	2	2	2	2	53~58,XY,+X,c	1	1	1	1	5	3-6-2013	2			5
704608F	Shaik Sanavulla	21	1	2013	11-1-2013	2	1	2	1	2	2	4.5	89	1	1	1	1	2	2	2	2	47~48,XY,+X,t	3	1	1	1	5	11-4-2013	2			5
659307F	Uttam Sahu	22	1	2013	8-28-2013	4	0	2	1	2	2	132	86	1	3	2	1	2	2	2	2	92,	5		1	1	5	8-29-2013	2			5
716037F	Mithun Biswas	22	1	2013	12-19-2013	0	0	2	1	2	2	3.3	90	1	1	1	1	2	2	2	2	46,XY[20]	5	1	1	1	5	12-19-2013	2			5
383051F	Mathew Jose	23	1	2013	1-9-2013	2	0	2	1	2	2	1.8	9	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	1-9-2013	2			5
664714F	Bahabood Kottarathil	23	1	2013	9-7-2013	4	0	2	1	2	2	31.7	96	1	1	1	1	2	2	2	2	45,XY,-9[4]/46	5	1	1	1	5	9-7-2013	1		3-7-2014	1
485375F	Shanti Prakash	25	1	2013	5-29-2013	0	0	2	1	2	2	0.4	57	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	5-31-2013	2		6-2-2013	2
606464F	Umesh Kumar Yada	26	1	2013	6-20-2013	0	0	2	3	2	2	1.7	84	1	3	2	2	3	3	3	3	46~47,XY,+Y,	3		1	1	5	6-22-2013	2		8-18-2013	2
402897F	Ranjan Giri	27	1	2013	2-2-2013	0	0	2	1	2	2	1.9	86	1	1	1	1	2	2	2	2	46,XY[20]	5	1	1	1	5	2-8-2013	2			5
427190F	Venkatachalam M	27	1	2013	3-6-2013	1	0	2	1	2	2	7.3	61.5	1	3	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	3-22-2013	2			5
479540F	Gaddamedi Ramesh	27	1	2013	5-15-2013	2	0	2	4	2	2	5.6	44	1	3	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	5-24-2013	2			5
496366F	Mohammed Rafri	27	1	2013	6-12-2013	0	0	1	3	2	1	7.2	12	1	1	2	1	2	2	2	2	8,add(16)(q24	3		1	1	5	6-12-2013	2			6
468847F	Kuppuswamy N	29	1	2013	7-3-2013	0	0	2	1	2	2	119.2	79	1	3	2	1	2	2	2	2	46,XY[20]	5		1	1	5	7-9-2013	2			5
460403F	Srinivas K	30	1	2013	4-24-2013	2	2	2	1	2	2	6.5	85	1	1	2	1	1	3	3	3	46,XY[20]	5	3	1	1	5	5-3-2013	2			5
763564F	Haris Iliath	30	1	2013	12-14-2013	3	0	2	1	2	2	7.3	59	1	3	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	12-14-2013	2			5
646731F	Guhanathan T	32	1	2013	8-20-2013	0	0	2	1	2	2	58.1	93	1	1	1	1	1	3	3	3	46,XY,t(1;21)(q34;q11.2)[1	3	3	1	1	5	8-20-2013	2			5

611569F	Kalyani Mukheree	33	1	2013	7-11-2013	0	0	2	1	1	3	4.4	87	1	3	2	2	3	3	3	3	'46,XX,del(1)(p	5		1	1	5	7-11-2013	2			5
628812F	Arun Sasidharan	33	1	2013	7-22-2013	0	0	2	1	2	2	110.2	98	1	3	2	1	2	2	2	2	46,XY[20]	5		1	1	5	7-23-2013	2			5
750427F	Dinakaran J	33	1	2013	12-31-2013	0	0	1	3	2	2	6.2	9	1	1	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	1-23-2014	2			5
650584F	Julbihar Ali	34	1	2013	8-19-2013	0	0	2	1	2	2	1.2	87	1	3	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	8-29-2013	2			5
677110F	Arvind Gadiya	34	1	2013	9-16-2013	0	0	1	6	2	2	135	31	1	3	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	9-16-2013	2		10-3-2013	2
373010F	Smitha Vargheese	35	2	2013	1-7-2013	2	3	2	1	2	3	2	63	1	1	2	2	3	3	3	3	46,XX[20]	5	1	1	1	5	6-16-2013	2			5
381164F	Binod Paswan	36	1	2013	1-4-2013	0	0	2	1	2	2	3.1	65	1	1	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	1-30-2013	2			5
406683F	Md Mizanur Rahman	37	1	2013	2-25-2013	0	0	2	1	2	2	45.1	91	1	3	2	2	3	3	3	3	46,XY[20]	5		1	1	5	3-1-2013	2			5
418895F	Ramesh A.K	37	1	2013	2-25-2013	4	2	1	3	2	2	11.4	71	1	3	2	2	3	3	3	3	Not Done	4	1	1	1	5	3-13-2013	2			5
659157F	Jimcy Joy	37	2	2013	8-29-2013	0	0	2	1	2	3	4.6	93	1	2	1	1	2	2	2	2	46,XX,add(19)(	5	1	1	1	5	9-2-2013	2			5
406148F	Gautam Das	38	1	2013	2-18-2013	2	3	2	1	2	2	12.5	100	1	1	1	1	2	2	2	2	45,XY,-7,-9,+m	3	1	1	1	5	2-19-2013	2		3-1-2013	2
482185F	Jeya Seelan P	38	1	2013	5-25-2013	0	5	2	1	2	2	1.7	71	1	3	2	1	2	2	2	2	45,XY,-7[13]/46	5	1	1	1	5	5-30-2013	2			5
635029F	Varghese George	38	1	2013	7-23-2013	0	0	2	1	2	2	1.9	94	1	1	2	1	2	2	2	2	Not Done	4		1	1	5	7-29-2013	2			5
630869F	Abul Wafa	39	1	2013	8-12-2013	0	0	2	1	2	2	9	95	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	8-12-2013	2			5
413215F	Mercy Clara	41	2	2013	2-14-2013	3	4	2	1	2	3	7.7	83	1	1	2	1	2	2	2	2	46,X,i(X;11)(p1	3	1	1	1	5	2-16-2013	2			5
447892F	Kumar s Rajeev	42	1	2013	4-2-2013	2	0	2	1	2	2	46.1	91	1	1	1	1	2	2	2	2	'47,XY,+X[11]/	1	1	1	1	5	4-3-2013	2			5
384430F	Mohammed Haniffa	44	1	2013	1-15-2013	0	0	2	1	2	2	8.3	96	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	1-26-2013	2			5
672100F	Kirti Kumar Srivastav	46	1	2013	9-10-2013	4	2	2	3	2	2	6.4	90	1	1	1	1	2	2	2	2	45,XY,-7[19]/46	5		1	1	5	9-11-2013	2			5
389139F	Narayayana Swamy	47	1	2013	1-22-2013	0	0	2	1	2	2	1	48	1	3	2	2	3	3	3	3	'45,X,-Y,del(2)(	3	1	1	1	5	2-1-2013	2			5
441097F	Bhaskar Raju	47	1	2013	2-4-2013	1	1	2	1	2	2	13.7	91.5	1	1	1	1	2	2	2	2	46,XY,del(9)(p1	5	1	1	1	5	4-1-2013	2			5
441392F	Sreeramulu Reddy N	47	1	2013	4-10-2013	3	0	2	1	2	2	1.9	91	1	1	2	1	2	2	2	2	51,X,+X,-Y,+4,	1	1	1	1	5	4-13-2013	2			5
713588F	Ilanchezian	48	1	2013	11-16-2013	1	0	2	3	2	2	0.9	69	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	11-29-2013	2			5
622582F	Karthikeyan A	50	1	2013	7-11-2013	0	0	2	1	2	2	4.7	90	1	1	2	1	2	2	2	2	'33~36<2n>,X'	3	1	1	1	5	7-14-2013	2			5
374584F	Sridharan S	52	1	2013	1-2-2013	0	0	2	1	2	2	4.8	72	1	2	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	1-11-2013	2			5
414598F	Attakoya	58	1	2013	2-15-2013	1	1	1	3	2	2	401.8	85	1	1	1	1	2	2	2	2	46,XY,t(2;7;10	5		1	1	5	2-15-2013	2			5
631330F	Mani Durai M.D.K	59	1	2013	7-23-2013	2	4	2	1	2	2	2.8	60	1	2	1	1	2	2	2	2	46,XY[20]	5	1	1	1	5	7-25-2013	2			5
429082F	Alagumani G	60	2	2013	3-28-2013	1	0	2	1	2	3	3.1	95	1	1	1	1	1	2	2	2	Complex karyo	3	3	1	1	5	3-30-2013	2			5
322434F	Rakesh Mir	20	1	2012	10-25-2012	4	0	1	3	2	2	13.4	55	1	1	1	1	2	2	2	1	Not Done	4	3	1	1	5	11-1-2012	2		1-20-2013	1
345465F	Tarak Nath Das	22	1	2012	11-14-2012	2	0	2	1	2	2	53.5	96	1	3	2	2	3	3	3	3	46,XY[20]	5	1	1	1	5	12-6-2012	2		11-26-2012	2
249851F	Rani Rajan	26	2	2012	7-18-2012	0	0	2	1	2	3	8.9	85	1	3	2	2	3	3	3	3	46,XX[20]	5	1	1	1	5	7-27-2012	2			5
317925F	Rakesh Benedict J	27	1	2012	10-8-2012	4	0	1	3	2	2	212.9	99	1	3	2	1	2	2	2	2	46,XY[12]	5		1	1	5	10-15-2012	2			5
327402F	Abdul Rasiq (adult)	27	1	2012	10-23-2012	0	0	2	1	2	2	0.4	51	1	1	2	1	1	3	3	3	46,XY[20]	5	3	1	1	5	10-23-2012	2			5
246418F	Prabavathi	30	2	2012	7-18-2012	0	0	1	2	1	3	9.6	21	1	3	2	2	3	3	3	3	Not Done	4	1	1	1	5	7-18-2012	2			5
377078F	Kencho Buthi	32	2	2012	12-27-2012	3	5	1	3	2	3	0.8	77	1	1	1	1	1	2	2	2	46,XX,t(9;22)(q	3	3	1	1	5	12-27-2012	1	6-10-2013		5
335844F	Pankaj Khan	34	1	2012	11-3-2012	6	8	1	1	2	2	203.4	96	1	3	2	2	3	3	3	3	46,XY[20]	5		1	1	5	11-3-2012	2			5
351396F	Arumugam M	39	1	2012	11-27-2012	0	2	2	1	2	2	2.7	82	1	1	2	1	2	2	2	2	46,XY[20]	5	1	1	1	5	12-3-2012	2			5
354964F	Parthiban	39	1	2012	12-6-2012	3	7	2	1	1	3	25.4	92.5	1	3	2	2	3	3	3	3	46,XY[19]	5		1	1	5	12-8-2012	2			5
367346F	Ceciliya	48	2	2012	12-18-2012	8	8	2	1	2	3	85.4	86	1	1	1	1	1	3	3	3	45~49,XX,+X,t	3	3	1	1	5	12-18-2012	2			5
847368D	Khamakhya Pada Ch	52	1	2012	7-20-2012	0	0	2	1	2	2	3.7	77	1	3	2	2	3	3	3	3	47,XY,+21[10]/	1		1	1	5	7-24-2012	2			5
209321F	Tapan Chandra Sarka	56	1	2012	9-20-2012	0	0	1	3	2	2	4.6	67	1	1	1	1	1	2	2	2	Not done	4	3	1	1	5	9-22-2012	2		10-23-2012	2
325914F	Shalini Devi	57	2	2012	11-3-2012	2	2	2	1	2	3	0.3	87	1	1	2	1	2	2	2	2	46,XX[20]	5		1	1	5	11-10-2012	2			5

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2-28-2014	2	0	702	2-28-2014	0	702
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3-7-2014	2	0	732	3-7-2014	0	732
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7-6-2012	8	0	6	7-6-2012	0	6
12-29-2012	2	1	197	12-29-2012	1	197
7-17-2012	5	1	111	7-17-2012	1	111
2-22-2014	5	1	592	2-22-2014	1	592
11-14-2012	5	1	175	11-14-2012	1	175
8-3-2012	5	1	39	8-3-2012	1	39
2-22-2013	5	1	258	2-22-2013	1	258
3-4-2014	2	0	633	3-4-2014	0	633
8-31-2012	2	1	218	8-31-2012	1	218
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9-28-2012	5	1	142	9-28-2012	1	142
2-14-2014	2	0	723	2-14-2014	0	723
9-27-2011	8	0	5		0	-40808
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1-31-2014	2	0	925		0	-40745
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2-18-2014	1	0	963		0	-40725
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5-17-2013	2	0	1154	5-17-2013	0	1154
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12-13-2013	1	0	1219	12-13-2013	0	1219
5-18-2012	5	1	565	5-18-2012	1	565
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1-10-2014	2	0	2538	1-10-2014	1	2538
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1-24-2014	1	0	2503	1-24-2014	0	2503
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11-23-2007	3	1	155	11-23-2007	1	155
6-26-2007	5	1	537	6-26-2007	1	537
6-21-2011	3	1	1938	6-29-2010	1	1581
11-23-2012	1	0	2338		0	-38898
6-25-2013	1	0	2435		0	-39015
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6-1-2007	5	1	335	1-16-2007	1	199
9-8-2006	5	1	22	9-5-2006	1	19
3-27-2007	2	0	214		0	-38954
3-20-2009	1	0	1137		0	-38755
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12-5-2012	5	1	2417	12-5-2012	1	2417
2-28-2014	1	0	2853		0	-38845
6-27-2006	7	1	23	7-27-2006	1	53
8-16-2013	1	0	2766		0	-38736
7-4-2007	5	1	436	1-11-2007	1	262
7-25-2008	2	0	761		0	-38893
8-9-2013	1	0	2592		0	-38903
7-24-2008	5	1	596	7-24-2008	1	596
11-18-2011	1	0	2123		0	-38742
2-14-2014	1	0	2689		0	-38995
11-20-2007	7	1	375	12-20-2007	1	405
1-13-2009	5	1	988	9-16-2008	1	869
8-5-2010	5	1	1401	3-8-2010	1	1251
9-24-2013	1	0	2811		0	-38730
2-18-2011	5	1	1576	12-30-2010	1	1526
5-18-2012	2	0	2271		0	-38776
3-17-2009	2	0	992		0	-38897
10-3-2006	7	1	68	10-3-2006	1	68
5-1-2008	2	0	588		0	-38981
10-26-2010	1	0	1560		0	-38917
12-17-2010	5	1	1465	4-20-2010	1	1224
3-10-2007	5	1	162	1-6-2007	1	99
4-1-2007	2	1	174	4-1-2007	1	174
9-4-2012	1	0	2092		0	-39064
4-18-2006	5	1	103	3-27-2006	1	81
7-16-2010	2	0	1399		0	-38976
10-22-2006	2	0	89		0	-38923

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12-8-2006	5	1	149	12-4-2006	1	145
8-18-2006	5	1	116	9-18-2006	1	147
1-5-2010	5	1	1135	12-29-2009	1	1128
5-4-2007	2	1	307	5-4-2007	1	307
7-2-2007	5	1	342	1-5-2007	1	164
3-5-2008	5	1	573	12-24-2007	1	501
11-12-2007	5	1	436	11-10-2007	1	434
7-22-2008	5	1	648	4-23-2008	1	558
9-1-2009	5	1	1034	1-29-2008	1	453
7-19-2007	5	1	247	9-7-2007	1	297
7-5-2007	2	1	296	7-5-2007	1	296
5-12-2007	5	1	306	5-12-2007	1	306
8-3-2007	2	0	441		0	-38856
6-12-2007	5	1	440	6-12-2007	1	440
2-25-2014	1	0	2784		0	-38911
1-22-2010	1	0	1409		0	-38791
11-2-2010	1	0	1916		0	-38568
1-19-2007	5	1	498	11-14-2006	1	432
10-22-2013	1	0	2847		0	-38722
5-16-2006	5	1	363	3-21-2006	1	307
2-10-2006	2	0	211		0	-38547
8-23-2007	3	1	622	7-23-2007	1	591
7-1-2005	7	1	22	8-1-2005	1	53
7-25-2006	5	1	248	6-8-2006	1	201
11-20-2007	2	0	1034		0	-38372
10-17-2006	5	1	622	9-8-2006	1	583
5-19-2006	5	1	401	5-5-2006	1	387
2-8-2013	1	0	2783		0	-38530
11-11-2011	1	0	2246		0	-38612
1-6-2007	3	1	595	12-11-2006	1	569
12-13-2013	1	0	2971		0	-38650
4-22-2008	2	0	979		0	-38581
1-22-2010	1	0	1543		0	-38657
6-2-2006	5	1	190	5-30-2006	1	187
2-10-2005	8	0	29		0	-38364
4-2-2013	1	0	2715		0	-38651
11-26-2010	1	0	1812		0	-38696
8-19-2005	5	1	186	6-18-2005	1	124
1-25-2011	5	1	1898	1-25-2011	1	1898
8-20-2013	1	0	2789		0	-38717
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5-16-2005	7	1	9	6-16-2005	1	40
1-7-2006	2	1	105	1-7-2006	1	105
6-10-2005	5	1	64	7-10-2005	1	94
10-8-2005	5	1	8	11-8-2005	1	39
2-14-2012	5	1	2394	6-1-2009	1	1406
1-9-2009	3	1	1395	1-25-2008	1	1045
2-25-2014	1	0	3178		0	-38517
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8-1-2008	5	1	1367	8-1-2008	1	1367
2-1-2011	1	0	2536	2-1-2011	0	2536
6-1-2010	1	0	2099	6-1-2010	0	2099
7-1-2005	5	1	252	7-1-2005	1	252
10-9-2009	2	0	1844	10-9-2009	0	1844
3-20-2014	2	0	3411	3-20-2014	1	3411
5-19-2006	5	1	506	5-19-2006	1	506
9-30-2008	2	0	1670	9-30-2008	0	1670
11-8-2005	2	0	621	11-8-2005	0	621
12-13-2013	2	0	3600	12-13-2013	0	3600
1-3-2006	5	1	445	1-3-2006	1	445
8-19-2005	2	1	283	8-19-2005	1	283
11-9-2012	1	0	3152	11-9-2012	0	3152
4-12-2005	5	1	408	4-12-2005	1	408
12-5-2008	1	0	1789	12-5-2008	0	1789
5-10-2005	5	1	418	5-10-2005	1	418
4-19-2005	5	1	377	4-19-2005	1	377
12-21-2005	5	1	383	12-21-2005	1	383
12-12-2008	1	0	1529	12-12-2008	0	1529
8-5-2008	5	1	1403	8-5-2008	1	1403
12-27-2011	2	0	2603	12-27-2011	0	2603
10-11-2013	1	0	3549	10-11-2013	0	3549
6-28-2011	1	0	2600	6-28-2011	0	2600
9-16-2004	5	1	181	9-16-2004	1	181
8-22-2008	5	1	1429	8-22-2008	1	1429
2-22-2005	2	0	144	2-22-2005	0	144
5-24-2005	5	1	346	5-24-2005	1	346
3-24-2005	2	1	134	3-24-2005	1	134
1-14-2005	5	1	289	1-14-2005	1	289
7-18-2005	8	0	248	7-18-2005	0	248
3-21-2014	2	0	64	3-21-2014	0	64
3-4-2014	2	0	27	3-4-2014	0	27
2-25-2014	2	0	20	2-25-2014	0	20
2-26-2014	2	0	26	2-26-2014	0	26
3-4-2014	2	0	26	3-4-2014	0	26
3-7-2014	2	0	144	3-7-2014	0	144
2-25-2014	2	0	356	2-25-2014	0	356
3-7-2014	2	0	123	3-7-2014	0	123
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3-7-2014	2	0	78	3-7-2014	0	78
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2-7-2014	5	1	153	2-7-2014	1	153
02-06-2013	7	1	2	02-06-2013	1	2
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9-24-2013	2	0	228	9-24-2013	0	228
2-25-2014	2	0	340	2-25-2014	0	340
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3-4-2014	2	0	80	3-4-2014	0	80
2-21-2014	2	0	185	2-21-2014	0	185

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2-21-2014	2	0	213	2-21-2014	0	213
1-23-2014	2	0	0	1-23-2014	0	0
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03-10-2013	7	1	17	03-10-2013	1	17
9-24-2013	2	0	100	9-24-2013	0	100
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2-25-2014	2	0	361	2-25-2014	0	361
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3-4-2014	2	0	183	3-4-2014	0	183
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1-17-2014	2	0	232	1-17-2014	0	232
3-21-2014	2	0	235	3-21-2014	0	235
3-4-2014	2	0	204	3-4-2014	0	204
3-22-2013	2	0	34	3-22-2013	0	34
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1-14-2014	2	0	368	1-14-2014	0	368
3-12-2013	8	0	25	3-12-2013	0	25
3-7-2014	2	0	225	3-7-2014	0	225
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12-20-2012	5	1	3	20-01-2013	1	3
11-26-2012	7	1	0	11-26-2012	1	0
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